* NOTICES *

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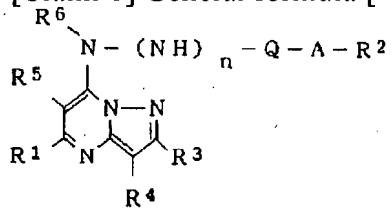
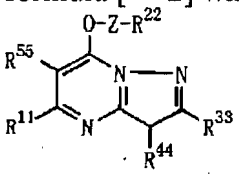
CLAIMS

[Claim(s)]
[Claim 1] General formula [** 1]



Among [type R1 as a hydrogen atom and a substituent A thienyl group, a lower alkoxy group, The low-grade alkyl group which has had a low-grade alkylthio group and oxo-radical, a carboxyl group, or hydroxyl, As a cycloalkyl radical, a thienyl group, a furil radical, a low-grade alkenyl radical, or a substituent, a low-grade alkyl group, The phenyl group which has had 1-3 of the radical chosen from a lower alkoxy group, a phenylthio radical, and a halogen atom R2 A naphthyl group, a cycloalkyl radical, a furil radical, a thienyl group, the pyridyl radical that has permuted by the halogen atom, As the phenoxy group which has permuted by the halogen atom, or a substituent, a low-grade alkyl group, A lower alkoxy group, a halogen atom, a nitro group, a halogenation low-grade alkyl group, A halogenation lower alkoxy group, a low-grade alkoxy carbonyl group, hydroxyl, A phenyl lower alkoxy group, the amino group, a cyano group, a low-grade alkanoloxy radical, The phenyl group which has had 1-3 of the radical chosen from a phenyl group and a JI low-grade alkoxy phosphoryl low-grade alkyl group R3 They are a hydrogen atom, a phenyl group, or a low-grade alkyl group R4 Hydrogen atom, A low-grade alkyl group and low-grade alkoxy carbonyl group, a phenyl low-grade alkyl group, The phenyl group or halogen atom which has had the phenylthio radical as a substituent R5 They are a hydrogen atom or a low-grade alkyl group R6 A hydrogen atom, a low-grade alkyl group, The benzoyl which has 1-3 of the radical chosen from a lower alkoxy group, a halogenation low-grade alkyl group, and a halogen atom as a phenyl low-grade alkyl group or a substituent is shown. R1 [moreover,] And R5 It may join together mutually and a low-grade alkylene group may be formed, Q shows a carbonyl group or a sulfonyl group, A shows single bond, a low-grade alkylene group, or a low-grade alkenylene group, respectively, and n shows 0 or 1.] The [1 and 5-pyrazolo a] pyrimidine derivative and general formula [** 2] which are come out of and expressed



R33, R44, and R55 show a hydrogen atom, and Z shows a low-grade alkylene group for the phenyl group in which R11 has a low-grade alkyl group among [type, and R22 has 1-3 of a lower alkoxy group as a substituent, respectively.] The adenosine enhancement agent characterized by containing the

effective dose with avirulent support by making at least one sort which comes out and is chosen from the [1 and 5-pyrazolo a] pyrimidine derivative expressed into an active principle.
[Claim 2] An active principle is the compound of a general formula (2) according to claim 1 and R4, and R5. And R6 A hydrogen atom, adenosine enhancement agent according to claim 1 as which Q is chosen from the compound of the general formula (1) according to claim 1 single bond and whose n a carbonyl group and A are 0.
[Claim 3] An active principle is R2. Adenosine enhancement agent according to claim 2 chosen from the compound of the general formula (1) according to claim 1 which is the phenyl group which has three of a lower alkoxy group as a substituent, and the compound of the general formula (2) according to claim 1 which is the phenyl group in which R22 has three of a lower alkoxy group as a substituent.
[Claim 4] An active principle is R1. Adenosine enhancement agent according to claim 3 chosen from the compound of the general formula (1) according to claim 1 which is n-propyl group or n-butyl, and the compound of the general formula (2) according to claim 1 whose R11 is n-butyl.
[Claim 5] An active principle A 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine, A 5-n-propyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine, 5 pyrazolo [-n-butyl-2-methyl-7-(3, 4, 5-trimethoxy benzoylamino)] [1 and 5-a] pyrimidine, And the adenosine enhancement agent according to claim 4 chosen from a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoyloxy) pyrazolo [1 and 5-a] pyrimidine.
[Claim 6] The adenosine enhancement agent according to claim 5 whose active principle is a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine.
[Claim 7] Prevention and the therapy agent of the myocardial infarction and/or cerebral infarction which are characterized by containing at least one sort of effective doses of the [1 and 5-pyrazolo a] pyrimidine derivative expressed with a general formula (1) and a general formula (2) according to claim 1 with avirulent support.
[Claim 8] Angina pectoris preventive characterized by containing at least one sort of effective doses of the [1 and 5-pyrazolo a] pyrimidine derivative expressed with a general formula (1) and a general formula (2) according to claim 1 with avirulent support.

[Translation done.]

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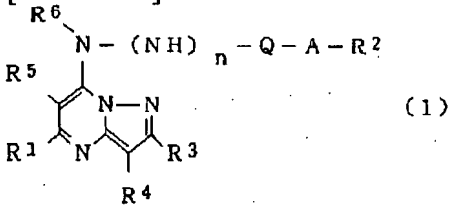
DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention relates to a new adenosine enhancement agent.
[0002]
[Description of the Prior Art] Myocardial infarction, cerebral infarction, etc. are known as a disease which increases in connection with aging. Although it is said that an organization originates in it being in an ischemia condition by lock out and constriction of a blood vessel, if an organization, especially the heart generally lapse into an ischemia condition, diseases, such as this, will be followed on the fall of blood fluid pressure, a microvessel will extend them, and the autogenous control ability which is going to maintain a fixed blood stream commits them. A deer is carried out and it is solved by this autogenous control ability that an adenosine has a role important as that regulator [J.Physiol., 204, and 317 (1963)].
[0003] That is, in the ischemia myocardium, the adenosine produced from ATP (adenosine triphosphate) which is an energy source, and it is based on the mechanism that this adenosine extends an arteriole.
[0004] Moreover, in addition to the above-mentioned arteriole escape operation, it is known by the adenosine that a vascularization operation and platelet aggregation depressant action are also shown, and the role of protection of an ischemia myocardium or reperfusion failure mitigation is also played in it.
[0005] Although the reproduced adenosine which carried out the deer was incorporated by the erythrocyte and the cardiac muscle cell and it disappeared quickly in response to decomposition by the enzyme, the drugs which control this and maintain the adenosine concentration of an organization gap, and the so-called adenosine enhancement agent were developed recently. As the typical thing, there are dipyridamole and dilazep, for example, this etc. is used as adjuvants, such as a nitrous-acid agent and a calcium antagonist, or use as a prophylactic of an anginal attack is considered.
[0006]
[Problem(s) to be Solved by the Invention] the purpose of this invention -- the above -- it is structurally unrelated in the compound which has well-known adenosine potentiation, and is in offering the adenosine enhancement agent using the matter and this which have the new adenosine potentiation which hardly has the side effect that compounds, such as this, moreover see.
[0007] Although this invention persons' research consortium had performed composition of various compounds and research of the pharmacological action which it has, an elucidation, etc. from sometime past for the purpose of development of a physic pharmaceutical preparation active principle compound, it succeeded in composition of a series of pyrazolo pyrimidine derivatives which have a powerful analgesic action previously in the process, and patent application of the invention concerning compounds, such as this, was carried out (WO 95/No. 35298 and WO 97/No. 11946).
[0008] In the continuing research, separate moreover, the compound of the above-mentioned single string [persons / this invention] has adenosine potentiation regardless of this operation with the analgesic action, and, moreover, this etc. newly came to complete this invention for a side effect being mitigated notably a header and here.
[0009]

[Means for Solving the Problem] That is, according to this invention, the adenosine enhancement agent which makes an active principle at least one sort chosen from the [1 and 5-pyrazolo a] pyrimidine derivative expressed with the following general formula (1) and a general formula (2) is offered.

[0010]

[Formula 3]

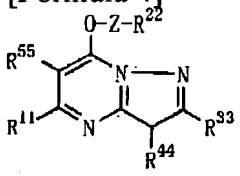


(1)

[0011] The inside of the above-mentioned general formula (1), and R1 As a hydrogen atom and a substituent, thienyl group, The low-grade alkyl group which has had a lower alkoxy group, low-grade alkylthio group, and oxo-radical, a carboxyl group, or hydroxyl, As a cycloalkyl radical, a thienyl group, a furil radical, a low-grade alkenyl radical, or a substituent, a low-grade alkyl group, The phenyl group which has had 1-3 of the radical chosen from a lower alkoxy group, a phenylthio radical, and a halogen atom R2 A naphthyl group, a cycloalkyl radical, a furil radical, a thienyl group, the pyridyl radical that has permuted by the halogen atom, As the phenoxy group which has permuted by the halogen atom, or a substituent, a low-grade alkyl group, A lower alkoxy group, a halogen atom, a nitro group, a halogenation low-grade alkyl group, A halogenation lower alkoxy group, a low-grade alkoxy carbonyl group, hydroxyl, A phenyl lower alkoxy group, the amino group, a cyano group, a low-grade alkanoloxy radical, The phenyl group which has had 1-3 of the radical chosen from a phenyl group and a JI low-grade alkoxy phosphoryl low-grade alkyl group R3 They are a hydrogen atom, a phenyl group, or a low-grade alkyl group R4 Hydrogen atom, A low-grade alkyl group and low-grade alkoxy carbonyl group, a phenyl low-grade alkyl group, The phenyl group or halogen atom which has had the phenylthio radical as a substituent R5 They are a hydrogen atom or a low-grade alkyl group R6 A hydrogen atom, a low-grade alkyl group, The benzoyl which has 1-3 of the radical chosen from a lower alkoxy group, a halogenation low-grade alkyl group, and a halogen atom as a phenyl low-grade alkyl group or a substituent is shown. Moreover, R1 And R5 It may join together mutually and a low-grade alkylene group may be formed, Q shows a carbonyl group or a sulfonyl group, A shows single bond, a low-grade alkylene group, or a low-grade alkenylene group, respectively, and n shows 0 or 1.

[0012]

[Formula 4]



(2)

[0013] R33, R44, and R55 show a hydrogen atom, and Z shows a low-grade alkylene group for the phenyl group in which R11 has a low-grade alkyl group among the above-mentioned general formula (2), and R22 has 1-3 of a lower alkoxy group as a substituent, respectively.

[0014] Each of each derivatives expressed with the above-mentioned general formula (1) and a general formula (2) is characterized in the point which the outstanding adenosine potentiation is shown and hardly shows side effects, such as common nausea and a common headache, dizziness, and feeling of heat, in the matter which moreover has this conventional seed adenosine potentiation.

[0015]

[Embodiment of the Invention] As each radical in the general formula (1) showing the active principle of this invention adenosine enhancement agent, each following radical can be illustrated, for example. That is, as a low-grade alkyl group, straight chains, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, and a hexyl group, or a branched chain-like low-grade alkyl group can be

illustrated.
[0016] As a cycloalkyl radical, cyclo propyl, cyclo butyl, cyclopentyl, cyclohexyl, cycloheptyl one, a cyclo octyl radical, etc. can be illustrated.
[0017] As a lower alkoxy group, methoxy and ethoxy ** propoxy, isopropoxy, butoxy one, pentyloxy one, a hexyloxy radical, etc. can be illustrated.
[0018] As a low-grade alkylthio group, a methylthio, ethyl thio, propyl thio, butyl thio, pentyl thio, a hexyl thio radical, etc. can be illustrated.
[0019] Fluorine, chlorine, a bromine, and iodine atom are included by the halogen atom.
[0020] As a halogenation low-grade alkyl group, trifluoromethyl, pentafluoroethyl, heptafluoro propyl, nona fluoro butyl, undeca fluoro pentyl, a trideca fluoro hexyl group, etc. can be illustrated.
[0021] As a halogenation lower alkoxy group, trifluoro methoxy and pentafluoro ethoxy ** heptafluoro propoxy, nona fluoro butoxy, undeca fluoro pentyloxy, a trideca fluoro hexyloxy radical, etc. can be illustrated.
[0022] As a low-grade alkoxy carbonyl group, methoxycarbonyl, ethoxycarbonyl, propoxy carbonyl, isopropoxycarbonyl, butoxycarbonyl, pentyloxy carbonyl, a hexyloxy carbonyl group, etc. can be illustrated.
[0023] As a JI low-grade alkoxy phosphoryl low-grade alkyl group, dimethoxy phosphoryl methyl, diethoxy phosphoryl methyl, dipropoxy phosphoryl methyl, diisopropoxy phosphoryl methyl, dibutoxy phosphoryl methyl, dipentyl oxy-phosphoryl methyl, dihexyl oxy-phosphoryl methyl, 2-(dimethoxy phosphoryl) ethyl, 2-(diethoxy phosphoryl) ethyl, 3-(diethoxy phosphoryl) propyl group, etc. can be illustrated.
[0024] 1-naphthyl and 2-naphthyl group are included by the naphthyl group.
[0025] As a low-grade alkylene group, methylene, ethylene, trimethylene, tetramethylen, pentamethylene, a hexamethylene radical, etc. can be illustrated.
[0026] Vinylene, a pro PENIREN radical, etc. can be illustrated as a low-grade alkenylene group.
[0027] As a pyridyl radical which has permuted by the halogen atom 2-pyridyl, 3-pyridyl, 4-pyridyl, 6-chloro-2-pyridyl, 5-chloro-2-pyridyl, 4-chloro-2-pyridyl, 3-chloro-2-pyridyl, 6-chloro-3-pyridyl, 5-chloro-3-pyridyl, 4-chloro-3-pyridyl, 2-chloro-3-pyridyl, 2-chloro-4-pyridyl, 3-chloro-4-pyridyl, 6-fluoro-3-pyridyl, 6-BUROMO-3-pyridyl, a 6-iodine-3-pyridyl radical, etc. can be illustrated.
[0028] As a phenoxy group which has permuted by the halogen atom, phenoxy, 2-chloro phenoxy, 3-chloro phenoxy, 4-chloro phenoxy, 4-fluorophenoxy, 4-BUROMO phenoxy, 4-iodine phenoxy group, etc. can be illustrated.
[0029] 2-thienyl and 3-thienyl group are included by the thienyl group, and 2-furil and 3-furil radical are included by the furil radical.
[0030] As a low-grade alkenyl radical, vinyl, an allyl compound, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 1-hexenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, a 5-hexenyl radical, etc. can be illustrated.
[0031] As a phenyl low-grade alkyl group, benzyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 4-phenyl butyl, 5-phenyl pentyl, 6-phenyl hexyl group, etc. can be illustrated.
[0032] As a phenyl lower alkoxy group, benzyloxy one, 2-phenylethoxy, 3-phenyl propoxy, 4-phenyl butoxy, 5-phenyl pentyloxy, 6-phenyl hexyloxy radical, etc. can be illustrated.
[0033] As a low-grade alkanoloxy radical, acetoxy, propionyloxy, butyryloxy, valeryloxy, pivaloyloxy one, hexanoyloxy, a heptanoyloxy radical, etc. can be illustrated.
[0034] As a low-grade alkyl group which has had a thienyl group, lower alkoxy group, low-grade alkylthio group, and oxo-radical, a carboxyl group, or hydroxyl as a substituent To the low-grade alkyl group which is not permuted [above-mentioned], in addition, 2-thienyl methyl, 3-thienyl methyl, 1-(2-thienyl) ethyl, 1-(3-thienyl) ethyl, 2-(2-thienyl) ethyl, 2-(3-thienyl) ethyl, 3-(2-thienyl) propyl, 4-(2-thienyl) butyl, 5-(2-thienyl) pentyl, 6-(2-thienyl) hexyl, methoxymethyl, Ethoxymethyl, propoxy methyl, butoxy methyl, pentyl oxymethyl, Hexyl oxymethyl, 1-methoxy ethyl, 2-methoxy ethyl, 3-methoxy propyl, 4-methoxy butyl, 5-methoxy pentyl, 6-methoxy hexyl, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 1-hydroxypropyl, 2-hydroxypropyl, 3-hydroxypropyl, 3-hydroxy butyl, 4-hydroxy pentyl,

5-hydroxy hexyl, methyl thiomethyl, ethyl thiomethyl, propyl thiomethyl, Butyl thiomethyl, pentyl thiomethyl, hexyl thiomethyl, 2-methylthio ethyl, 3-methylthiopropyl, 4-methylthio butyl, 5-methylthio pentyl, 6-methylthio hexyl, the formyl, formyl methyl, acetyl, 2-formyl ethyl, 2-oxo-propyl, a propionyl, 3-formyl propyl, 3-oxo-butyl, 2-oxo-butyl, the butyryl, 4-formyl butyl, 4-oxo-pentyl, 3-oxo-pentyl, 2-oxo-pentyl, valeryl, 5-formyl pentyl, 5-oxo-hexyl, 4-oxo-hexyl, 3-oxo-hexyl, 2-oxo-hexyl, Hexa noil, carboxymethyl, 2-carboxyethyl, 3-carboxypropyl, 4-carboxy butyl, 5-carboxy pentyl, 6-carboxy hexyl group, etc. can be illustrated.

[0035] As a phenyl group which has had 1-3 of the radical chosen from a low-grade alkyl group, a lower alkoxy group, a phenylthio radical, and a halogen atom as a substituent Phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethyl phenyl, 4-propyl phenyl, 4-buthylphenyl, 4-t-buthylphenyl, 4-pentyl phenyl, 4-hexyl phenyl, 2, 3-dimethylphenyl, 2, 4-dimethylphenyl, 2, 5-dimethylphenyl, 2, 6-dimethylphenyl, 3, 4-dimethylphenyl, 3, 5-dimethylphenyl, 2-methoxypheny, 3-methoxypheny, 4-methoxypheny, 4-ethoxy phenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxy phenyl, 4-hexyloxy phenyl, 2, 3-dimethoxy phenyl, 2, 4-dimethoxy phenyl, 2, 5-dimethoxy phenyl, 2, 6-dimethoxy phenyl, 3, 4-dimethoxy phenyl, 3, 5-dimethoxy phenyl, 3 and 4, 5-trimethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 4-BUROMO phenyl, 4-iodine phenyl, 4-fluoro phenyl, 4-(phenylthio) phenyl, 3-(phenylthio) phenyl, 2-(phenylthio) phenyl group, etc. can be illustrated.

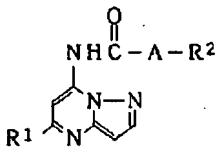
[0036] Each following radical can be illustrated as a phenyl group which has had 1-3 of the radical chosen from a low-grade alkyl group, a lower alkoxy group, a halogen atom, a nitro group, a halogenation low-grade alkyl group, a halogenation lower alkoxy group, a low-grade alkoxy carbonyl group, hydroxyl, a phenyl lower alkoxy group, the amino group, a cyano group, a low-grade alkanoloxy radical, a phenyl group, and a JI low-grade alkoxy phosphoryl low-grade alkyl group as a substituent.

[0037] Namely, phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethyl phenyl, 4-propyl phenyl, 4-buthylphenyl, 4-t-buthylphenyl, 4-pentyl phenyl, 4-hexyl phenyl, 2-methoxypheny, 3-methoxypheny, 4-methoxypheny, 4-ethoxy phenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxy phenyl, 4-hexyloxy phenyl, 2, 3-dimethoxy phenyl, 2, 4-dimethoxy phenyl, 2, 5-dimethoxy phenyl, 2, 6-dimethoxy phenyl, 3, 4-dimethoxy phenyl, 3, 5-dimethoxy phenyl, 2 and 3, 4-trimethoxyphenyl, 2, 3, 5-trimethoxyphenyl, 2 and 3, 6-trimethoxyphenyl, 2, 4, 5-trimethoxyphenyl, 2 and 4, 6-trimethoxyphenyl, 3, 4, 5-trimethoxyphenyl, 3 and 4, 5-TORIETOKISHI phenyl, 2-fluoro phenyl, 3-fluoro phenyl, 4-fluoro phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-BUROMO phenyl, 3-BUROMO phenyl, 4-BUROMO phenyl, 4-iodine phenyl, 2, 3-dichlorophenyl, 2, 4-dichlorophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-trifluoro methylphenyl, 3-trifluoro methylphenyl, 4-trifluoro methylphenyl, 4-pentafluoroethyl phenyl, 4-heptafluoro propyl phenyl, 4-nona fluoro buthylphenyl, 4-undeca fluoro pentyl phenyl, 4-trideca fluoro hexyl phenyl, 2-methoxycarbonyl phenyl, 3-methoxycarbonyl phenyl, 4-methoxycarbonyl phenyl, 4-ethoxycarbonyl phenyl, 4-propoxy carbonylphenyl, 4-butoxycarbonyl phenyl, 4-pentyloxy carbonylphenyl, 4-hexyloxy carbonylphenyl, 2-biphenyl, 3-biphenyl, 4-biphenyl, 2-(diethoxy phosphoryl methyl) phenyl, 3-(diethoxy phosphoryl methyl) phenyl, 4-(diethoxy phosphoryl methyl) phenyl, 4-(dimethoxy phosphoryl methyl) phenyl, 4-(diisopropoxy phosphoryl methyl) phenyl, 3, 5-dimethoxy-4-ethoxy phenyl, 3, 5-dimethoxy-4-propoxy phenyl, 4-butoxy - 3, 5-dimethoxy phenyl, 3, 5-dimethoxy-4-pentyloxy phenyl, 3, 5-dimethoxy-4-hexyloxy phenyl, 2, 3-bis(trifluoromethyl) phenyl, 2, 4-bis(trifluoromethyl) phenyl, 2, 5-bis (trifluoromethyl) phenyl, 2, 6-bis(trifluoromethyl) phenyl, 3, 4-bis(trifluoromethyl) phenyl, 3, 5-bis (trifluoromethyl) phenyl, 3, 5-dimethoxy-4-hydroxyphenyl, 3, 5-diethoxy-4-hydroxyphenyl, 3, 5-dipropoxy-4-hydroxyphenyl, 4-benzyloxy - 3, 5-dimethoxy phenyl, 4-benzyloxy - 3, 5-diethoxy phenyl, 3, 5-dimethoxy-4-(2-phenylethoxy) phenyl, 4-acetoxy -3, 5-dimethoxy phenyl, 3, 5-dimethoxy-4-propionyloxy phenyl, 2-chloro -3, 5-dimethoxy phenyl, 4-chloro -3, 5-dimethoxy phenyl, 4-BUROMO - 3, 5-dimethoxy phenyl, 3, 5-dimethoxy-4-iodine phenyl, 3, 5-dichloro-4-methoxypheny, 3, 5-dichloro-4-ethoxy phenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 4-trifluoro methoxypheny, 3-trifluoro methoxypheny, 2-trifluoro methoxypheny, 4-pentafluoro ethoxy phenyl, 4-heptafluoro propoxy phenyl, 4-nona fluoro butoxy phenyl, 4-undeca fluoro pentyloxy phenyl, 4-trideca fluoro hexyloxy phenyl, 3, 5-bis(trifluoro methoxy) phenyl, 3 and 4, 5-tris

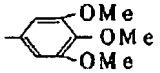
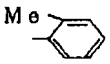
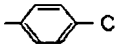
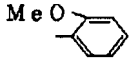
(trifluoro methoxy) phenyl group, etc. can be illustrated.
[0038] As a phenyl group which has had the phenylthio radical as a substituent, phenyl, 4-(phenylthio) phenyl, 3-(phenylthio) phenyl, 2-(phenylthio) phenyl group, etc. can be illustrated.
[0039] As benzoyl which has 1-3 of the radical chosen from a lower alkoxy group, a halogenation low-grade alkyl group, and a halogen atom as a substituent 2-chloro benzoyl, 3-chloro benzoyl, 4-chloro benzoyl, 2-fluoro benzoyl, 2-BUROMO benzoyl, 2-iodine benzoyl, 2, 4-dichlorobenzoyl, 3, 4-dichlorobenzoyl, 2, 5-dichlorobenzoyl, 2, 6-dichlorobenzoyl, 2-trifluoro methylbenzoyl, 3-trifluoro methylbenzoyl, 4-trifluoro methylbenzoyl, 3, 5-bis(trifluoromethyl) benzoyl, 3 and 4, 5-tris (trifluoromethyl) benzoyl, 2-methoxy benzoyl, 3-methoxy benzoyl, 4-methoxy benzoyl, 2, 3-dimethoxybenzoyl, 2, 4-dimethoxybenzoyl, 3, 5-dimethoxybenzoyl, 3, 4, 5-trimethoxybenzoyl, 2-ethoxy benzoyl, 2-propoxy benzoyl, 2-butoxy benzoyl, 2-pentyloxy benzoyl, 2-hexyloxy benzoyl, etc. can be illustrated.
[0040] As each radical in the general formula (2) showing the active principle of this invention adenosine enhancement agent, each following radical can be illustrated, for example. That is, as a low-grade alkyl group, straight chains, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, and a hexyl group, or a branched chain-like low-grade alkyl group can be illustrated.
[0041] As a low-grade alkylene group, methylene, ethylene, ethylidene, trimethylene, tetramethylen, pentamethylene, hexamethylene, etc. can be illustrated.
[0042] As a phenyl group which has 1-3 of a lower alkoxy group as a substituent 2-methoxypheny, 3-methoxypheny, 4-methoxypheny, 4-ethoxy phenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxy phenyl, 4-hexyloxy phenyl, 2, 4-dimethoxy phenyl, 3, 4-dimethoxy phenyl, 3, 5-dimethoxy phenyl, 2 and 4, 5-trimethoxyphenyl, 3 and 4, 5-trimethoxyphenyl, 2 and 4, 6-trimethoxyphenyl, 4-ethoxy -3, 5-dimethoxy phenyl group, etc. can be illustrated.
[0043] The [1 and 5-pyrazolo a] pyrimidine derivative expressed with a general formula (1) and (2) is useful to the therapy and prevention of myocardial infarction or cerebral infarction as an adenosine enhancement agent. And there is no side effect with this derivative common to the conventional adenosine enhancement agent, and it does not have a possibility of bringing about a hallucination, distraction, etc. or causing addiction and habituation, either.
[0044] As a [1 and 5-pyrazolo a] pyrimidine derivative desirable as the above-mentioned adenosine enhancement agent active principle, the compound of a general formula (2) and R4, and R5 and R6 can illustrate the compound of the general formula (1) single bond and whose n a carbonyl group and A are 0 for a hydrogen atom and Q.
[0045] The compound of the general formula (1) which is the phenyl group in which (a) R2 have three of a lower alkoxy group as a substituent also especially among the desirable [1 and 5-pyrazolo a] pyrimidine derivatives, such as this, And the compound of the general formula (2) which is the phenyl group in which R22 has three of a lower alkoxy group as a substituent is more suitable. Also among them, it is R1. The compound of the general formula (1) which is n-propyl group or n-butyl, and especially the compound of the general formula (2) whose R11 is n-butyl are suitable.
[0046] As an example of the most desirable [1 and 5-pyrazolo a] pyrimidine derivative A 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine, A 5-n-propyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine, 5 pyrazolo [-n-butyl-2-methyl-7-(3, 4, 5-trimethoxy benzoylamino)] [1 and 5-a] pyrimidine, And a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoyloxy) pyrazolo [1 and 5-a] pyrimidine can be illustrated. The 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine is the optimal also among them.
[0047] this invention active principle compound expressed with a general formula (1) can be manufactured by various kinds of approaches, and can illustrate the approach of a publication as the example, for example in said WO 95/No. 35298 official report.
[0048] this invention active principle compound can be obtained by obtaining the 7-hydroxy [1 and 5-pyrazolo a] pyrimidines, carrying out the condensation reaction of suitable carboxylate and the 3-amino pyrazoles, halogenating this subsequently, carrying out to the 7-halogeno [1 and 5-pyrazolo a] pyrimidines typically, processing this by aqueous ammonia or the hydrazine further, changing into 7-

amino object, and making a halogenide react to this.
[0049] this invention active principle compound expressed with a general formula (2) can also be manufactured by various kinds of approaches. As the example, the approach of a publication can be illustrated, for example in said WO 97/No. 11946 official report.
[0050] this invention active principle compound expressed with a general formula (2) can be obtained by obtaining the 7-halogeno [1 and 5-pyrazolo a] pyrimidines, and making the suitable, alcoholic derivative for this as well as the compound of the above-mentioned general formula (1) react typically.
[0051] In this way, as an example of the active principle compound of this invention adenosine enhancement agent obtained, each compound shown in the 1st table of the following - the 6th table as examples 1-136 can be illustrated.
[0052]
[Table 1]

第 1 表

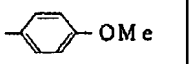
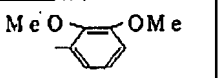
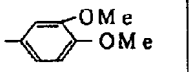
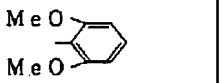
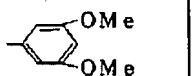
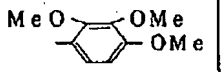
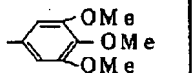
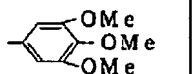
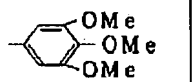
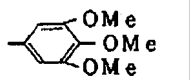
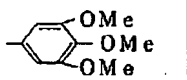


Me：メチル基、Et：エチル基、nPr：n－プロピル基、
nBu：n－ブチル基、nPe：n－ペンチル基、Ph：フェニル基

実施例No.	R^1	R^2	A	融点 (℃)（再結晶溶媒）
1	nBu		単結合	127～129（ジエチルエーテル－n－ヘキサン）
2	nBu	Ph	単結合	83～85（酢酸エチル－n－ヘキサン）
3	nBu		単結合	102～104（n－ヘキサン）
4	nBu		単結合	94～95（n－ヘキサン）
5	nBu		単結合	83～84（n－ヘキサン）
6	nBu		単結合	^{1}H－NMR（$CDCl_3$） 0.97(3H,t,J=7.3), 1.37(9H,s), 1.4-1.5(2H,m), 1.7-1.9(2H,m), 2.86(2H,t,J=7.8), 6.57(1H,d,J=2.3), 7.58(1H,d,J=8.7), 7.77(1H,s), 7.97(1H,d,J=8.7), 8.03(1H,d,J=2.3), 10.0(1H,brs)
7	nBu		単結合	82～84（n－ヘキサン）
8	nBu		単結合	49～51（n－ヘキサン）

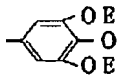
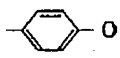
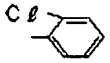
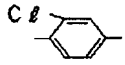
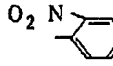
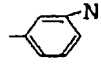
[0053]
[Table 2]

第 1 表 (続き)

実施例No.	R1	R2	A	融点 (℃) (再結晶溶媒)
9	nBu		単結合	108～109 (n－ヘキサン)
10	nBu		単結合	129～132 (n－ヘキサン)
11	nBu		単結合	143～144 (ジエチルエーテル－n－ヘキサン)
12	nBu		単結合	101～103 (ジエチルエーテル－n－ヘキサン)
13	nBu		単結合	92～94 (ジエチルエーテル－n－ヘキサン)
14	nBu		単結合	115～117 (酢酸エチル－n－ヘキサン)
15	Et		単結合	141～143 (酢酸エチル－n－ヘキサン)
16	nPr		単結合	119～121 (ジエチルエーテル－n－ヘキサン)
17			単結合	198～201 (酢酸エチル－n－ヘキサン)
18	nPe		単結合	116～118 (n－ヘキサン)
19	Ph		単結合	185～187 (酢酸エチル－n－ヘキサン)

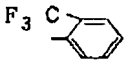
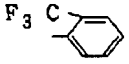
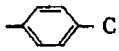
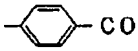
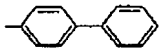
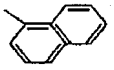
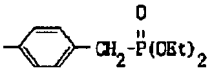
[0054]
[Table 3]

第 1 表 (続き)

実施例No.	R^1	R^2	A	融点 (℃) (再結晶溶媒)
20	nBu		単結合	100～102 (ジエチルエーテル－n－ヘキサン)
21	nBu		単結合	87～90 (n－ヘキサン)
22	nBu		単結合	99～100 (n－ヘキサン)
23	nBu		単結合	107～109 (ジエチルエーテル)
24	nBu		単結合	81～82 (n－ヘキサン)
25	nBu		単結合	92～94 (ジエチルエーテル)
26	nBu		単結合	97～99 (n－ヘキサン)
27	nBu		単結合	93～95 (n－ヘキサン)
28	nBu		単結合	97～99 (n－ヘキサン)
29	nBu		単結合	133～135 (酢酸エチル－n－ヘキサン)
30	nBu		単結合	143～145 (酢酸エチル－n－ヘキサン)

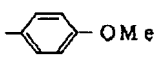
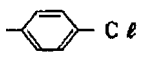
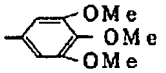
[0055]
[Table 4]

第 1 表 (続き)

実施例No.	R1	R2	A	融点 (℃) (再結晶溶媒)
31	Et		単結合	125～127 (ジエチルエーテル－n－ヘキサン)
32	nBu		単結合	84～87 (n－ヘキサン)
33	nBu		単結合	95～97 (n－ヘキサン)
34	nBu		単結合	122～123 (n－ヘキサン)
35	nBu		単結合	139～141 (酢酸エチル－n－ヘキサン)
36	nBu		単結合	119～121 (酢酸エチル－n－ヘキサン)
37	nBu		単結合	57～60 (酢酸エチル－n－ヘキサン)
38	nBu		単結合	82～84 (ジエチルエーテル－n－ヘキサン)
39	nBu		単結合	103～105 (酢酸エチル－n－ヘキサン)
40	nBu		単結合	92～93 (ジエチルエーテル－n－ヘキサン)
41	nBu	Ph	$-CH_2-$	80～82 (ジエチルエーテル－n－ヘキサン)

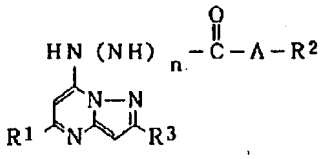
[0056]
[Table 5]

第 1 表 (続き)

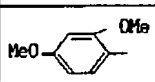
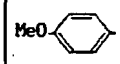
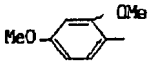
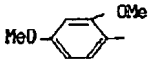
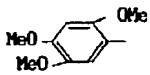
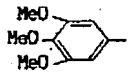
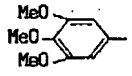
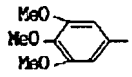
実施例No.	R^1	R^2	A	融点 (℃) (再結晶溶媒)
42	nBu		$-CH_2-$	73～75 (ジエチルエーテル－n－ヘキサン)
43	nBu	Ph	$-C_2H_4-$	^1H－NMR ($CDCl_3$) 0.95(3H,t,J=7.3), 1.3-1.5 (2H,m), 1.7-1.8(2H,m), 2.80 (2H,t,J=7.8), 2.88(2H,t,J=7.5), 3.09(2H,t,J=7.5), 6.53 (1H,d,J=2.2), 7.2-7.3(5H,m), 7.60(1H,s), 7.95(1H,d,J=2.2), 9.23(1H,brs)
44	nBu	PhO－	$-CH_2-$	108～109 (n－ヘキサン)
45	nBu		$-CH_2-$	140～142 (酢酸エチル－n－ヘキサン)
46	nBu		-CH=CH-	134～137 (酢酸エチル－n－ヘキサン)

[0057]
[Table 6]

第　2　表

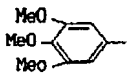
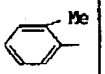
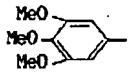
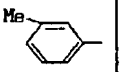
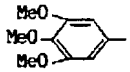
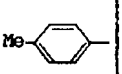
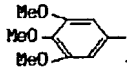
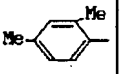
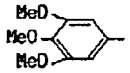
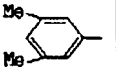
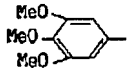
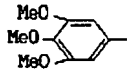
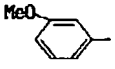
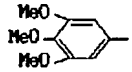
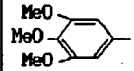
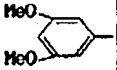
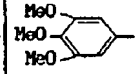
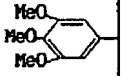
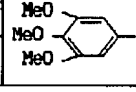


Me：メチル基、Et：エチル基、nPr：n－プロピル基、
nBu：n－ブチル基、tBu：t－ブチル基、nPe：n－ペンチル基、
Ph：フェニル基、Ac：アセチル基

実施例No.	R1	R2	R3	A	n	融　点（℃）（再結晶溶媒）
47	nBu		H	単結合	0	^{1}H－NMR（CDCℓ$_3$）0.95(3H,t,J-7.4), 1.2-2.1(14H,m), 2.4-2.6(1H,m),2.81(2H,t,J-7.8), 6.54(1H,d,J-2.2),7.62(1H,s), 8.00(1H,d,J-2.2),9.29(1H,brs)
48	nBu		H	単結合	0	141～142（エタノール－n－ヘキサン）
49			H	単結合	0	209～211（塩化メチレン－酢酸エチル）
50			H	単結合	0	206～208（塩化メチレン－酢酸エチル）
51	nBu		H	単結合	0	136～137（エタノール－n－ヘキサン）
52	Me		H	単結合	0	173～175（エタノール－n－ヘキサン）
53	nBu		Me	単結合	0	127～129（エタノール－n－ヘキサン）
54			H	単結合	0	104～106（酢酸エチル－n－ヘキサン）

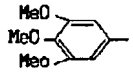
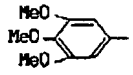
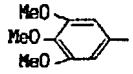
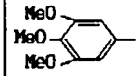
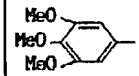
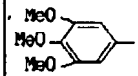
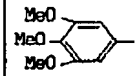
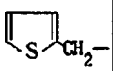
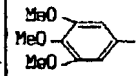
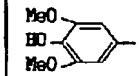
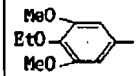
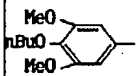
[0058]
[Table 7]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
55	Et-O-CH_2-		H	単結合	0	138～140 (酢酸エチル－n－ヘキサン)
56			H	単結合	0	163～165 (クロロホルム－酢酸エチル)
57			H	単結合	0	166～168 (酢酸エチル－n－ヘキサン)
58			H	単結合	0	193～195 (塩化メチレン－ジエチルエーテル)
59			H	単結合	0	174～176 (塩化メチレン－ジエチルエーテル)
60			H	単結合	0	203～205 (塩化メチレン－ジエチルエーテル)
61			H	単結合	0	175～177 (塩化メチレン－酢酸エチル)
62			H	単結合	0	192～194 (塩化メチレン－ジエチルエーテル)
63			H	単結合	0	181～183 (塩化メチレン－ジエチルエーテル)
64			H	単結合	0	224～226 (塩化メチレン－ジエチルエーテル)
65			H	単結合	0	214～216 (塩化メチレン－ジエチルエーテル)

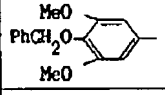
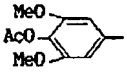
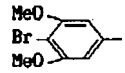
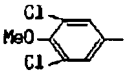
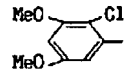
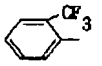
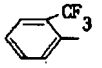
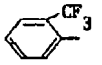
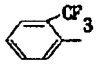
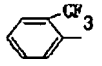
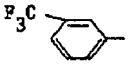
[0059]
[Table 8]

第 2 表 (続き)

実施例No	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
66			H	単結合	0	190～192 (塩化メチレン－ジエチルエーテル)
67			H	単結合	0	222～224 (クロロホルム－酢酸エチル)
68			H	単結合	0	193～195 (クロロホルム－酢酸エチル)
69			H	単結合	0	189～191 (塩化メチレン－ジエチルエーテル)
70			H	単結合	0	174～176 (塩化メチレン－酢酸エチル)
71			H	単結合	0	191～193 (塩化メチレン－ジエチルエーテル)
72			H	単結合	0	198～200 (塩化メチレン－酢酸エチル)
73			H	単結合	0	157～159 (酢酸エチル)
74	nBu		H	単結合	0	159～161 (エタノール－n－ヘキサン)
75	nBu		H	単結合	0	79～81 (ジエチルエーテル－n－ヘキサン)
76	nBu		H	単結合	0	98～100 (n－ヘキサン)

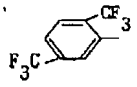
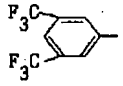
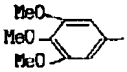
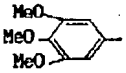
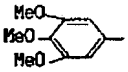
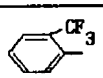
[0060]
[Table 9]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
77	nBu		H	単結合	0	82～85 (エタノール－n－ヘキサン)
78	nBu		H	単結合	0	158～160 (酢酸エチル－n－ヘキサン)
79	nBu		H	単結合	0	182～184 (酢酸エチル－n－ヘキサン)
80	nBu		H	単結合	0	132～135 (酢酸エチル－n－ヘキサン)
81	nBu		H	単結合	0	111～113 (ジエチルエーテル－n－ヘキサン)
82	Me		H	単結合	0	154～155 (エタノール－n－ヘキサン)
83	nPr		H	単結合	0	139～141 (ジエチルエーテル－n－ヘキサン)
84			H	単結合	0	102～104 (n－ヘキサン)
85	nPe		H	単結合	0	93～95 (n－ヘキサン)
86	Ph		H	単結合	0	143～145 (ジエチルエーテル－n－ヘキサン)
87	nBu		H	単結合	0	46～48 (酢酸エチル－n－ヘキサン)

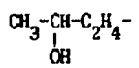
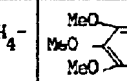
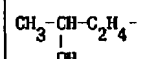
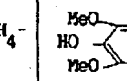
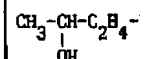
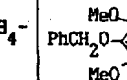
[0061]
[Table 10]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
88	nBu		H	単結合	0	108～110 (n-ヘキサン)
89	nBu		H	単結合	0	92.5～94.5 (n-ヘキサン)
90	nBu		H	単結合	0	106～108 (n-ヘキサン)
91	nBu		H	単結合	0	123～125 (エタノール-n-ヘキサン)
92	nBu		H	単結合	0	123～125 (ジエチルエーテル-n-ヘキサン)
93	nBu		H	単結合	0	139～140 (エタノール-n-ヘキサン)
94	nBu		H	CH_2	0	121～123 (酢酸エチル-n-ヘキサン)
95	nBu		H	-CH=CH-	0	194～196 (エタノール-n-ヘキサン)
96	nBu		H	単結合	1	222 (分解) (エタノール-n-ヘキサン)
97	Ph		H	単結合	1	250 (分解) (メタノール-n-ヘキサン)
98	nBu		H	単結合	1	247 (分解) (エタノール-n-ヘキサン)

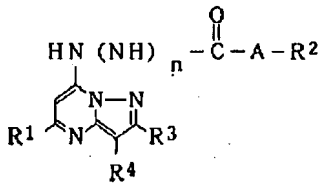
[0062]
[Table 11]

第 2 表 (続き)

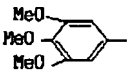
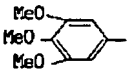
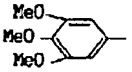
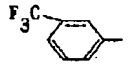
実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
99	Ph		H	単結合	1	263 (分解) (エタノール-n-ヘキサン)
100			H	単結合	0	128～130 (塩化メチレン-n-ヘキサン)
101			H	単結合	0	153～155 (エタノール-n-ヘキサン)
102			H	単結合	0	127～129 (酢酸エチル-n-ヘキサン)

[0063]
[Table 12]

第　3　表

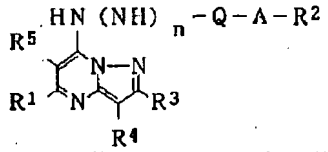


Me：メチル基、nBu：n－ブチル基、

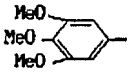
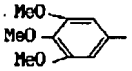
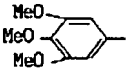
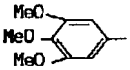
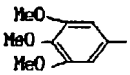
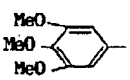
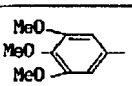
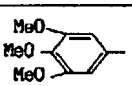
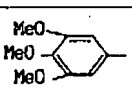
実施例No.	R^1	R^2	R^3	R^4	A	n	融点（℃）（再結晶溶媒）
103	nBu		Me	Cl	単結合	0	106～108（エタノール－n－ヘキサン）
104	nBu		H	Cl	単結合	0	142～143（エタノール－n－ヘキサン）
105	nBu		H	Br	単結合	0	146～148（エタノール－n－ヘキサン）
106	nBu		H	Cl	単結合	0	133～135（ジエチルエーテル－n－ヘキサン）

[0064]
[Table 13]

第 4 表

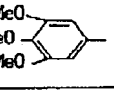
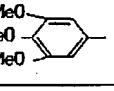
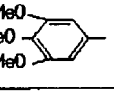
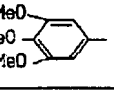
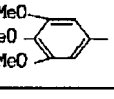
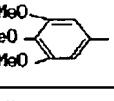
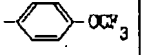
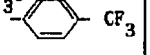


Me：メチル基、Et：エチル基、nBu：n－ブチル基、Ph：フェニル基

実施例No.	R^1	R^5	R^2	R^3	R^4	Q	A	n	融点 (℃) (再結晶溶媒)
107	H	H		H	H	O ‖ C	単結合	0	185～187 (塩化メチレン－n－ヘキサン)
108	nBu	H		Me		O ‖ C	単結合	0	138～140 (酢酸エチル－n－ヘキサン)
109	nBu	H		nBu	H	O ‖ C	単結合	0	95～97 (酢酸エチル－n－ヘキサン)
110	nBu	H		nBu	Me	O ‖ C	単結合	0	96～98 (酢酸エチル－n－ヘキサン)
111	nBu	H		Ph	H	O ‖ C	単結合	0	190～192 (塩化メチレン－ジエチルエーテル)
112	nBu	H		Ph	$PhCH_2$-	O ‖ C	単結合	0	149～151 (酢酸エチル n－ヘキサン)
113	nBu	H		Ph		O ‖ C	単結合	0	111～113 (酢酸エチル－n－ヘキサン)
114	nBu	H		H	nBu	O ‖ C	単結合	0	81～83 (n－ヘキサン)
115	nBu	H		H	Ph	O ‖ C	単結合	0	139～141 (酢酸エチル－n－ヘキサン)

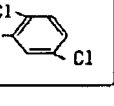
[0065]
[Table 14]

第 4 表 (続き)

実施例No.	R^1	R^5	R^2	R^3	R^4	Q	A	n	融点 (℃) (再結晶溶媒)
116	nBu	Me		H	H	O ‖ C	単結合	0	145～147 (塩化メチレン－n－ヘキサン)
117	$-CH_2CH_2CH_2CH_2-$			H	H	O ‖ C	単結合	0	102～104 (塩化メチレン－n－ヘキサン)
118	$Me-\overset{O}{\overset{\|\|}{C}}-CH_2CH_2-$	H		H	H	O ‖ C	単結合	0	115～117 (塩化メチレン－n－ヘキサン)
119	$Et-S-CH_2-$	H		H	H	O ‖ C	単結合	0	80～82 (酢酸エチル－n－ヘキサン)
120	$MeS-CH_2CH_2-$	H		H	H	O ‖ C	単結合	0	113～115 (塩化メチレン－ジエチルエーテル)
121	PhS-	H		H	H	O ‖ C	単結合	0	179～181 (塩化メチレン－ジエチルエーテル)
122	nBu	H		H	H	O ‖ C	単結合	0	98～100 (ジエチルエーテル)
123	nBu	H		H	H	O ‖ C	単結合	0	73～75 (n－ヘキサン)
124	nBu	H		H	H	O ‖ C	単結合	0	129～131 (n－ヘキサン)
125	nBu	H		H	H	O ‖ C	単結合	0	91～93 (ジエチルエーテル n－ヘキサン)
126	nBu	H		H	H	O ‖ C	単結合	0	91～93 (n－ヘキサン)

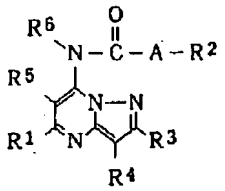
[0066]
[Table 15]

第 4 表 (続き)

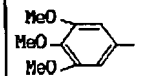
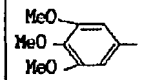
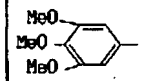
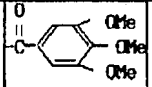
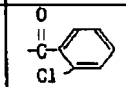
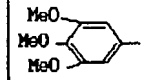
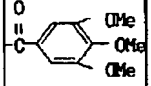
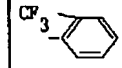
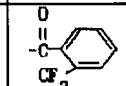
実施例No.	R^1	R^5	R^2	R^3	R^4	Q	A	n	融点 (℃) (再結晶溶媒)
127	nBu	H	Ph	H	H	SO_2	単結合	0	300℃以上 (酢酸エチル－n－ヘキサン)
128	nBu	H		H	H	SO_2	単結合	0	300℃以上 (酢酸エチル－n－ヘキサン)

[0067]
[Table 16]

第 5 表

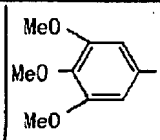


Me：メチル基、nBu：n－ブチル基

実施例No	R1	R5	R2	R3	R4	R6	A	融点（℃）（再結晶溶媒）
129	nBu	H		H	H	Me	単結合	93～95（酢酸エチル－n－ヘキサン）
130	nBu	H		H	H	Ph-CH_2-	単結合	^{1}H-NMR($CDCl_3$) 0.76(3H,t,J=7.2), 0.9-1.1(2H,m), 1.3-1.4(2H,m), 2.51(2H,t,J=7.4), 3.47(6H,s), 3.74(3H,s), 5.33(2H,brs), 5.83(1H,s), 6.60(2H,s), 6.68(1H,d,J=2.0), 7.1-7.3(5H,m), 8.24(1H,d,J=2.0)
131	nBu	H		H	H		単結合	127～129（酢酸エチル－n－ヘキサン）
132	nBu	H		H	H		単結合	119～121（ジエチルエーテル－n－ヘキサン）
133	Me	H		H	H		単結合	180～182（塩化メチレン－n－ヘキサン）
134	nBu	H		H	H		単結合	111～113（ジエチルエーテル－n－ヘキサン）

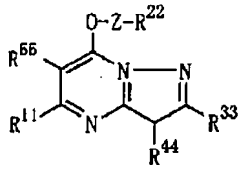
[0068]
[Table 17]

第 5 表 （続き）

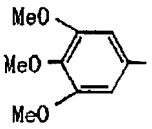
実施例No.	R 1	R 5	R 2	R 3	R 4	R 6	A	融点（℃）（再結晶溶媒）
135	HOOC-C_3H_6-	H		H	H	H	単結合	191-193（エタノール－n－ヘキサン）

[0069]
[Table 18]

第 6 表



Ｍｅ：メチル基、ｎ－Ｂｕ：ｎ－ブチル基

実施例No.	R^{11}	R^{22}	R^{33}	R^{44}	R^{55}	Z	融点 (℃) (再結晶溶媒)
136	n-Bu		H	H	H	$-CH_2-$	100-103 (酢酸エチル-ｎ－ヘキサン)

[0070] Each compound expressed with a general formula (1) and a general formula (2) can be made into the acid addition salt permitted in physic, and salts, such as this, are also included by the active principle compound of this invention adenosine enhancement agent. As an acid in which the above-mentioned acid addition salt may be made to form, organic acids, such as inorganic acids, such as a hydrochloric acid, a hydrobromic acid, and a sulfuric acid, oxalic acid, a fumaric acid, a maleic acid, a tartaric acid, and a citric acid, can be illustrated, for example, and the formation reaction of this acid addition salt can follow a conventional method.

[0071] Moreover, the inside of the compound expressed with a general formula (1) and R6 What is a hydrogen atom can make this copper salt, such as alkaline-earth-metal salts, for example, a calcium salt, such as an alkali-metal salt, for example, sodium salt, and potassium salt, and magnesium salt, etc. according to a conventional method, and salts, such as this, are also included by the active principle compound of this invention adenosine enhancement agent.

[0072] In addition, the inside of the compound expressed with a general formula (1), the compound whose A is an alkenylene group, and R1 Some compounds which are low-grade alkenyl radicals can take cis- ** trans-isomer structure, and this invention adenosine enhancement agent can make all, such as this, an active principle.

[0073] Moreover, the optical isomer which made the carbon atom the asymmetric center exists in the part in the compound expressed with a general formula (1), and this invention adenosine enhancement agent can make an active principle both this optically active substance and racemic modification.

[0074] This is used for this invention adenosine enhancement agent with suitable avirulent pharmaceutical preparation support by making into an active principle at least one sort chosen from the compound expressed with the compound and general formula (2) which are expressed with a general formula (1), and it is made into the gestalt of a common physic pharmaceutical preparation constituent, and is used.

[0075] A diluent or excipients, such as the bulking agent usually used according to the use gestalt of pharmaceutical preparation as the above-mentioned pharmaceutical preparation support used for this invention physic pharmaceutical preparation, an extending agent, a binder, moisture adhesive material, disintegrator, a surface active agent, and lubricant, can be illustrated, and selection use of these is suitably carried out according to the administration unit form voice of the pharmaceutical preparation obtained.

[0076] As administration unit form voice of the above-mentioned physic pharmaceutical preparation, various kinds of gestalten can choose according to the therapy purpose, and a tablet, a pill, powder, liquids and solutions, suspension, an emulsion, a granule, a capsule, suppositories, injections (liquids and solutions, suspension, etc.), an ointment, etc. are mentioned as the typical thing.

[0077] It faces fabricating in the gestalt of a tablet. As the above-mentioned pharmaceutical preparation

support For example, a lactose, White soft sugar, a sodium chloride, grape sugar, a urea, starch, a calcium carbonate, Excipients, such as a kaolin, crystalline cellulose, a silicic acid, and potassium phosphate, water, Ethanol, propanol, simple syrup, grape-sugar liquid, starch liquid, A gelatin solution, a carboxymethyl cellulose, hydroxypropylcellulose, Binders, such as methyl cellulose and a polyvinyl pyrrolidone, carboxymethylcellulose sodium, Carboxymethyl-cellulose calcium, hydroxypropylcellulose, Desiccation starch, sodium alginate, agar powder, the end of a laminaran, Disintegrator, such as a sodium hydrogencarbonate and a calcium carbonate, and polyoxyethylene sorbitan fatty acid ester Surfactants, such as sodium lauryl sulfate and a stearic acid monoglyceride, Collapse inhibitors, such as white soft sugar, stearin, cocoa butter, and hydrogenated oil, a quarternary-ammonium-salt radical, Lubricant, such as a polyethylene glycol, etc. can be used in adsorbents, such as moisturizers, such as absorption enhancers, such as sodium lauryl sulfate, a glycerol, and starch, starch, a lactose, a kaolin, a bentonite, and a colloid silicic acid, purification talc, a stearate, and the end of a boric acid. Furthermore, a tablet can be used as the tablet which gave the usual coating if needed, for example, a sugar-coated tablet, a gelatin encapsulation lock, an enteric tablet, a film coated tablet or an auxiliary rim lock, and a multilayered tablet.

[0078] It faces fabricating in the gestalt of a pill and disintegrator, such as binders, such as excipients, such as grape sugar, a lactose, starch, cacao butter, hardening vegetable oil, a kaolin, and talc, gummi arabicum pulveratum, powdered tragacanth, gelatin, and ethanol, a laminaran, and agar, etc. can be used as pharmaceutical preparation support.

[0079] It faces fabricating in the gestalt of suppositories and the ester of a polyethylene glycol, cacao butter, higher alcohol, and higher alcohol, gelatin, semisynthetic glyceride, etc. can be used as pharmaceutical preparation support.

[0080] A capsule is mixed with various kinds of pharmaceutical preparation support which usually illustrated the active principle compound of this invention above according to the conventional method, and is filled up with and adjusted to a hard gelatine capsule, an elasticity capsule, etc.

[0081] When prepared as injections, such as liquids and solutions, an emulsion, and suspension, it can be sterilized, and as for this etc., it is desirable that they are blood and an isotonicity, and it is faced fabricating in gestalten, such as this, and can use water, ethyl alcohol, macro gall, propylene glycol, ethoxylation isostearyl alcohol, polyoxy-ized isostearyl alcohol, and polyoxyethylene sorbitan fatty acid ester as a diluent. In addition, the salt, the grape sugar, or the glycerol of sufficient amount to adjust an isosmotic solution in this case may be made to contain in this invention drugs, and the usual solubilizing agent, a buffer, an aponia-ized agent, etc. may be added.

[0082] Furthermore, a coloring agent, a preservative, perfume, a flavor agent, a sweetening agent, etc. and other drugs can also be made to contain in this invention drugs if needed.

[0083] It faces fabricating in the gestalt of ointments, such as a paste, a cream, and gel, and white vaseline, a paraffin, a glycerol, a cellulosic, a polyethylene glycol, silicon, a bentonite, etc. can be used as a diluent.

[0084] Although especially the amount of the active principle compound expressed with the general formula (1) and general formula (2) which should be contained in this invention drugs is not limited but is suitably chosen from a large area, it is usually good in physic pharmaceutical preparation to contain about about 1 to 70% of the weight.

[0085] Especially the medication method of the above-mentioned physic pharmaceutical preparation does not have a limit, and is determined according to various formulation, a patient's age, the conditions of sex and others, extent of a disease, etc. for example, a tablet, a pill, liquids and solutions, suspension, an emulsion, a granule, and a capsule administer orally -- having -- injections -- independent -- or it mixes with the usual water additions, such as grape sugar and amino acid, and administers intravenously -- having -- further -- the need -- responding -- independent -- the inside of intramuscular and a hide, and hypodermically -- or intraperitoneal administration is carried out and intrarectal administration of the suppositories is carried out.

[0086] Although the dose of the above-mentioned physic pharmaceutical preparation is suitably chosen by the direction for use, a patient's age, the conditions of sex and others, extent of a disease, etc., it is

good for the amount of this invention compound which is usually an active principle to set to about about 0.5-20mg per weight per day of 1kg, and it can prescribe this pharmaceutical preparation for the patient in 1 - 4 steps on the 1st.
[0087]
[Example] Hereafter, in order to explain this invention in more detail, the example of preparation of this invention adenosine enhancement agent is given, and, subsequently the example of a pharmacological test is given.
[0088]
[The example 1 of preparation] The hard gelatine capsule (1000 pieces) contained 250mg per capsule was prepared by the next formula, using a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine as a preparation active principle compound of a capsule.
[0089]
An active principle compound 250g crystalline cellulose (Japanese pharmacopoeia article) 30g corn starch (Japanese pharmacopoeia article) 17g talc (Japanese pharmacopoeia article) 2g magnesium stearate (Japanese pharmacopoeia article) 1g, i.e., each component, was finely used as powder, the gelatine capsule for internal use which has a desired dimension after mixing was enough filled up so that it might become a homogeneous mixture, and the target capsule was prepared.
[0090]
[The example 2 of preparation] The tablet (2000 locks) contained 300mg per one lock was prepared by the next formula, using a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine as a preparation active principle compound of a tablet.
[0091]
An active principle compound 600g lactose (Japanese pharmacopoeia article) 67g corn starch (Japanese pharmacopoeia article) 33g carboxymethyl-cellulose calcium (Japanese pharmacopoeia article) 25g methyl cellulose (Japanese pharmacopoeia article) 12g magnesium stearate (Japanese pharmacopoeia article) According to 3g, i.e., the above-mentioned formula, an active principle compound, a lactose, corn starch, and carboxymethyl-cellulose calcium are mixed enough. Mixture was granulated using the methyl cellulose water solution, the screen of 24 meshes was mixed with through, this was mixed with magnesium stearate, it pressed in the tablet, and the target tablet was prepared.
[0092]
[The example 1 of a pharmacological test] The Hartley (Hartley) system male guinea pig (10 weeks old, 400-450g) was slaughtered by cervical dislocation, the ileum was taken out, and the surrounding organization was exfoliated. The ileum was carved into die length of 3-4cm, it hung under the pressure of 1g during the organ bath which put in 10ml (NaCl 118mM, KCl 4.7mM, CaCl2 2.5mM, KH2PO4 1.2mM, MgSO4 1.2mM, NaHCO3 25mM, glucose 11mM) of Krebs-Henseleit solutions, and aeration of the O2-/CO2 (95% / 5%) mixed gas was carried out continuously.
[0093] Adding the electrical stimulation of 25V to this ileum with the period of 0.1Hz, the adenosine was cumulatively added from 10-8M during the organ bath, and it asked for the adenosine concentration by which the twitch Mr. contraction by electrical stimulation is controlled 100% (control group).
[0094] In addition, twitch Mr. contraction was measured in AISO tonic transformer DEYUSA (isotonic transducer, the Nihon Kohden make, TD-111T), and was recorded by the recorder (NIHON DENSI KAGAKU, U-228).
[0095] On the other hand, 30 quotas which add an adenosine were asked for the adenosine concentration which adds during the organ bath and by which the twitch Mr. contraction by electrical stimulation is controlled [M / 10-6M (this invention group 1) or / (this invention group 2) / 3x10-6] 100% in a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine like the above.
[0096] Consequently, the adenosine concentration by which contraction is controlled 100% was set to 10-6M by this invention group 1, and was set to 3x10-7M by this invention group 2, and it fell to 1/3 and 1/10 compared with the control group, respectively. this invention active principle compound became clear [that the outstanding adenosine potentiation is shown] from this.
[0097]

[The example 2 of a pharmacological test] The Hartley (Hartley) system male guinea pig (10 weeks old, 400-450g) was slaughtered by cervical dislocation, the heart was taken out, and the atrium was separated. this after checking that the atrium has contracted spontaneously -- a Krebs-Henseleit solution (NaCl [ ] -- 118 mM) KCl 4.7 -- mM and CaCl2 2.5mM and KH2PO4 1.2 mM MgSO4 1.2 -- mM and NaHCO3 25mM and glucose It hung under the pressure of 1g during the organ bath which put in 10ml of 11mM(s), and aeration of the O2-/CO2 (95% / 5%) mixed gas was carried out continuously.
[0098] The adenosine was cumulatively added from 3x10-7M during the organ bath, and it asked for the adenosine concentration by which spontaneous contraction of an atrium begins to be controlled (control group).
[0099] In addition, spontaneous contraction of an atrium was measured in AISO tonic transformer DEYUSA (isotonic transducer, the Nihon Kohden make, TD-111T), and after amplifying with living body amplifier (Nihon Kohden, TB-611T), it was recorded by the recorder (NIHON DENSI KAGAKU, U-228).
[0100] On the other hand, ten quotas which add an adenosine were asked for the adenosine concentration which adds during the organ bath and by which spontaneous contraction of an atrium begins to be controlled [M / 3x10-6M (this invention group 1) or / (this invention group 2) / 10-5] in a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine like the above.
[0101] Consequently, the adenosine concentration by which contraction begins to be controlled 100% was set to 3x10-7M by this invention group 1, and was set to 10-7M by this invention group 2, and it fell to 1/10 and 1/30 compared with the control group, respectively. this invention active principle compound became clear [that the outstanding adenosine potentiation is shown] from this.
[0102]
[The example 3 of a pharmacological test] The longitudinal muscle was exfoliated, after having slaughtered the Hartley (Hartley) system male guinea pig (10 weeks old, 350-400g) by cervical dislocation, taking out the ileum and removing contents and an unnecessary organization. The longitudinal muscle which exfoliated was attached in the cannula which fixed the electrode, aeration of the O2-/CO2 (95% / 5%) mixed gas was carried out, and it hung in Magnus tubing which filled the Krebs-Henseleit solution (NaCl 118.3mM, KCl 4.7mM, CaCl2 2.5mM, KH2PO4 1.2mM, MgSO4 1.2mM, NaHCO3 25.0mM, glucose 11.1mM) which kept it warm at 37 degrees C. In addition, the longitudinal muscle prevented from touching a direct electrode.
[0103] When SUTIMYURETA (diamond medical system company make, DPS-06 mold) was used for the above-mentioned longitudinal muscle, the electrical stimulation of the square wave for period [of 0.1Hz] and persistence time 0.5 m seconds was added and nerve-stimulus contraction was stabilized, the adenosine was cumulatively added from 0.1microM in the Krebs-Henseleit solution, and IC50 of nerve-stimulus contraction depressant action was calculated.
[0104] The IC50 above-mentioned value was calculated from the adenosine concentration of two points, and the rate of control before and after 50% of rates of control. In addition, nerve-stimulus contraction was measured using FD pickup (the Nihon Kohden Corp. make, TB-611T mold) and amplifier (the Nihon Kohden Corp. make, AP-601G mold).
[0105] On the other hand, as a sample offering compound, it adds to five quotas which add an adenosine by the concentration of 1microM by using as a dimethyl sulfoxide solution the compound shown in said each table, and they were asked for IC50 of the nerve-stimulus contraction depressant action of an adenosine like the above. And whenever [enhancement] was computed by having calculated the ratio of IC50 at the time of sample offering compound un-adding to this value.
[0106] A result is shown in the 7th table of the following.
[0107]
[Table 19]

供試化合物(実施例番号)	増強度
1	4．8
16	7．6
19	6．9
53	8．4
55	5．1
75	6．0
100	2．7
111	2．7
135	2．6
136	7．1

[0108] this invention active principle compound became clear [that the outstanding adenosine potentiation is shown] from the above-mentioned table.

[Translation done.]

* NOTICES *

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2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

TECHNICAL FIELD

[Field of the Invention] This invention relates to a new adenosine enhancement agent.

[Translation done.]

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PRIOR ART

[Description of the Prior Art] Myocardial infarction, cerebral infarction, etc. are known as a disease which increases in connection with aging. Although it is said that an organization originates in it being in an ischemia condition by lock out and constriction of a blood vessel, if an organization, especially the heart generally lapse into an ischemia condition, diseases, such as this, will be followed on the fall of blood fluid pressure, a microvessel will extend them, and the autogenous control ability which is going to maintain a fixed blood stream commits them. A deer is carried out and it is solved by this autogenous control ability that an adenosine has a role important as that regulator [J.Physiol., 204, and 317 (1963)].
[0003] That is, in the ischemia myocardium, the adenosine produced from ATP (adenosine triphosphate) which is an energy source, and it is based on the mechanism that this adenosine extends an arteriole.
[0004] Moreover, in addition to the above-mentioned arteriole escape operation, it is known by the adenosine that a vascularization operation and platelet aggregation depressant action are also shown, and the role of protection of an ischemia myocardium or reperfusion failure mitigation is also played in it.
[0005] Although the reproduced adenosine which carried out the deer was incorporated by the erythrocyte and the cardiac muscle cell and it disappeared quickly in response to decomposition by the enzyme, the drugs which control this and maintain the adenosine concentration of an organization gap, and the so-called adenosine enhancement agent were developed recently. As the typical thing, there are dipyridamole and dilazep, for example, this etc. is used as adjuvants, such as a nitrous-acid agent and a calcium antagonist, or use as a prophylactic of an anginal attack is considered.

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TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] the purpose of this invention -- the above -- it is structurally unrelated in the compound which has well-known adenosine potentiation, and is in offering the adenosine enhancement agent using the matter and this which have the new adenosine potentiation which hardly has the side effect that compounds, such as this, moreover see.
[0007] Although this invention persons' research consortium had performed composition of various compounds and research of the pharmacological action which it has, an elucidation, etc. from sometime past for the purpose of development of a physic pharmaceutical preparation active principle compound, it succeeded in composition of a series of pyrazolo pyrimidine derivatives which have a powerful analgesic action previously in the process, and patent application of the invention concerning compounds, such as this, was carried out (WO 95/No. 35298 and WO 97/No. 11946).
[0008] In the continuing research, separate moreover, the compound of the above-mentioned single string [persons / this invention] has adenosine potentiation regardless of this operation with the analgesic action, and, moreover, this etc. newly came to complete this invention for a side effect being mitigated notably a header and here.

[Translation done.]

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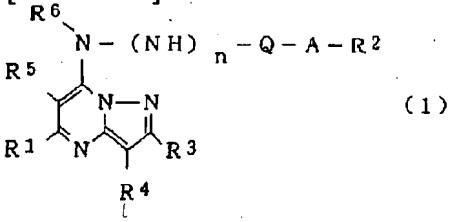
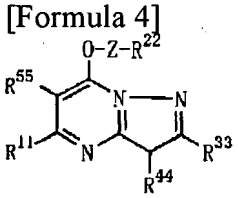
MEANS

[Means for Solving the Problem] That is, according to this invention, the adenosine enhancement agent which makes an active principle at least one sort chosen from the [1 and 5-pyrazolo a] pyrimidine derivative expressed with the following general formula (1) and a general formula (2) is offered.
[0010]
[Formula 3]



(1)

[0011] The inside of the above-mentioned general formula (1), and R1 As a hydrogen atom and a substituent, thienyl group, The low-grade alkyl group which has had a lower alkoxy group, low-grade alkylthio group, and oxo-radical, a carboxyl group, or hydroxyl, As a cycloalkyl radical, a thienyl group, a furil radical, a low-grade alkenyl radical, or a substituent, a low-grade alkyl group, The phenyl group which has had 1-3 of the radical chosen from a lower alkoxy group, a phenylthio radical, and a halogen atom R2 A naphthyl group, a cycloalkyl radical, a furil radical, a thienyl group, the pyridyl radical that has permuted by the halogen atom, As the phenoxy group which has permuted by the halogen atom, or a substituent, a low-grade alkyl group, A lower alkoxy group, a halogen atom, a nitro group, a halogenation low-grade alkyl group, A halogenation lower alkoxy group, a low-grade alkoxy carbonyl group, hydroxyl, A phenyl lower alkoxy group, the amino group, a cyano group, a low-grade alkanoloxy radical, The phenyl group which has had 1-3 of the radical chosen from a phenyl group and a JI low-grade alkoxy phosphoryl low-grade alkyl group R3 They are a hydrogen atom, a phenyl group, or a low-grade alkyl group R4 Hydrogen atom, A low-grade alkyl group and low-grade alkoxy carbonyl group, a phenyl low-grade alkyl group, The phenyl group or halogen atom which has had the phenylthio radical as a substituent R5 They are a hydrogen atom or a low-grade alkyl group R6 A hydrogen atom, a low-grade alkyl group, The benzoyl which has 1-3 of the radical chosen from a lower alkoxy group, a halogenation low-grade alkyl group, and a halogen atom as a phenyl low-grade alkyl group or a substituent is shown. Moreover, R1 And R5 It may join together mutually and a low-grade alkylene group may be formed, Q shows a carbonyl group or a sulfonyl group, A shows single bond, a low-grade alkylene group, or a low-grade alkenylene group, respectively, and n shows 0 or 1.
[0012]
[Formula 4]



(2)

[0013] R33, R44, and R55 show a hydrogen atom, and Z shows a low-grade alkylene group for the phenyl group in which R11 has a low-grade alkyl group among the above-mentioned general formula (2), and R22 has 1-3 of a lower alkoxy group as a substituent, respectively.
[0014] Each of each derivatives expressed with the above-mentioned general formula (1) and a general formula (2) is characterized in the point which the outstanding adenosine potentiation is shown and hardly shows side effects, such as common nausea and a common headache, dizziness, and feeling of heat, in the matter which moreover has this conventional seed adenosine potentiation.
[0015]
[Embodiment of the Invention] As each radical in the general formula (1) showing the active principle of this invention adenosine enhancement agent, each following radical can be illustrated, for example. That is, as a low-grade alkyl group, straight chains, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, and a hexyl group, or a branched chain-like low-grade alkyl group can be illustrated.
[0016] As a cycloalkyl radical, cyclo propyl, cyclo butyl, cyclopentyl, cyclohexyl, cycloheptyl one, a cyclo octyl radical, etc. can be illustrated.
[0017] As a lower alkoxy group, methoxy and ethoxy ** propoxy, isopropoxy, butoxy one, pentyloxy one, a hexyloxy radical, etc. can be illustrated.
[0018] As a low-grade alkylthio group, a methylthio, ethyl thio, propyl thio, butyl thio, pentyl thio, a hexyl thio radical, etc. can be illustrated.
[0019] Fluorine, chlorine, a bromine, and iodine atom are included by the halogen atom.
[0020] As a halogenation low-grade alkyl group, trifluoromethyl, pentafluoroethyl, heptafluoro propyl, nona fluoro butyl, undeca fluoro pentyl, a trideca fluoro hexyl group, etc. can be illustrated.
[0021] As a halogenation lower alkoxy group, trifluoro methoxy and pentafluoro ethoxy ** heptafluoro propoxy, nona fluoro butoxy, undeca fluoro pentyloxy, a trideca fluoro hexyloxy radical, etc. can be illustrated.
[0022] As a low-grade alkoxy carbonyl group, methoxycarbonyl, ethoxycarbonyl, propoxy carbonyl, isopropoxycarbonyl, butoxycarbonyl, pentyloxy carbonyl, a hexyloxy carbonyl group, etc. can be illustrated.
[0023] As a JI low-grade alkoxy phosphoryl low-grade alkyl group, dimethoxy phosphoryl methyl, diethoxy phosphoryl methyl, dipropoxy phosphoryl methyl, diisopropoxy phosphoryl methyl, dibutoxy phosphoryl methyl, dipentyl oxy-phosphoryl methyl, dihexyl oxy-phosphoryl methyl, 2-(dimethoxy phosphoryl) ethyl, 2-(diethoxy phosphoryl) ethyl, 3-(diethoxy phosphoryl) propyl group, etc. can be illustrated.
[0024] 1-naphthyl and 2-naphthyl group are included by the naphthyl group.
[0025] As a low-grade alkylene group, methylene, ethylene, trimethylene, tetramethylen, pentamethylene, a hexamethylene radical, etc. can be illustrated.
[0026] Vinylene, a pro PENIREN radical, etc. can be illustrated as a low-grade alkenylene group.
[0027] As a pyridyl radical which has permuted by the halogen atom 2-pyridyl, 3-pyridyl, 4-pyridyl, 6-chloro-2-pyridyl, 5-chloro-2-pyridyl, 4-chloro-2-pyridyl, 3-chloro-2-pyridyl, 6-chloro-3-pyridyl, 5-chloro-3-pyridyl, 4-chloro-3-pyridyl, 2-chloro-3-pyridyl, 2-chloro-4-pyridyl, 3-chloro-4-pyridyl, 6-fluoro-3-pyridyl, 6-BUROMO-3-pyridyl, a 6-iodine-3-pyridyl radical, etc. can be illustrated.
[0028] As a phenoxy group which has permuted by the halogen atom, phenoxy, 2-chloro phenoxy, 3-chloro phenoxy, 4-chloro phenoxy, 4-fluorophenoxy, 4-BUROMO phenoxy, 4-iodine phenoxy group, etc. can be illustrated.
[0029] 2-thienyl and 3-thienyl group are included by the thienyl group, and 2-furil and 3-furil radical are included by the furil radical.
[0030] As a low-grade alkenyl radical, vinyl, an allyl compound, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 1-hexenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, a 5-hexenyl radical, etc. can be illustrated.
[0031] As a phenyl low-grade alkyl group, benzyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 4-

phenyl butyl, 5-phenyl pentyl, 6-phenyl hexyl group, etc. can be illustrated.
[0032] As a phenyl lower alkoxy group, benzyloxy one, 2-phenylethoxy, 3-phenyl propoxy, 4-phenyl butoxy, 5-phenyl pentyloxy, 6-phenyl hexyloxy radical, etc. can be illustrated.
[0033] As a low-grade alkanoloxy radical, acetoxy, propionyloxy, butyryloxy, valeryloxy, pivaloyloxy one, hexanoyloxy, a heptanoyloxy radical, etc. can be illustrated.
[0034] As a low-grade alkyl group which has had a thienyl group, lower alkoxy group, low-grade alkylthio group, and oxo-radical, a carboxyl group, or hydroxyl as a substituent To the low-grade alkyl group which is not permuted [above-mentioned], in addition, 2-thienyl methyl, 3-thienyl methyl, 1-(2-thienyl) ethyl, 1-(3-thienyl) ethyl, 2-(2-thienyl) ethyl, 2-(3-thienyl) ethyl, 3-(2-thienyl) propyl, 4-(2-thienyl) butyl, 5-(2-thienyl) pentyl, 6-(2-thienyl) hexyl, methoxymethyl, Ethoxymethyl, propoxy methyl, butoxy methyl, pentyl oxymethyl, Hexyl oxymethyl, 1-methoxy ethyl, 2-methoxy ethyl, 3-methoxy propyl, 4-methoxy butyl, 5-methoxy pentyl, 6-methoxy hexyl, hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 1-hydroxypropyl, 2-hydroxypropyl, 3-hydroxypropyl, 3-hydroxy butyl, 4-hydroxy pentyl, 5-hydroxy hexyl, methyl thiomethyl, ethyl thiomethyl, propyl thiomethyl, Butyl thiomethyl, pentyl thiomethyl, hexyl thiomethyl, 2-methylthio ethyl, 3-methylthiopropyl, 4-methylthio butyl, 5-methylthio pentyl, 6-methylthio hexyl, the formyl, formyl methyl, acetyl, 2-formyl ethyl, 2-oxo-propyl, a propionyl, 3-formyl propyl, 3-oxo-butyl, 2-oxo-butyl, the butyryl, 4-formyl butyl, 4-oxo-pentyl, 3-oxo-pentyl, 2-oxo-pentyl, valeryl, 5-formyl pentyl, 5-oxo-hexyl, 4-oxo-hexyl, 3-oxo-hexyl, 2-oxo-hexyl, Hexa noil, carboxymethyl, 2-carboxyethyl, 3-carboxypropyl, 4-carboxy butyl, 5-carboxy pentyl, 6-carboxy hexyl group, etc. can be illustrated.
[0035] As a phenyl group which has had 1-3 of the radical chosen from a low-grade alkyl group, a lower alkoxy group, a phenylthio radical, and a halogen atom as a substituent Phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethyl phenyl, 4-propyl phenyl, 4-buthylphenyl, 4-t-buthylphenyl, 4-pentyl phenyl, 4-hexyl phenyl, 2, 3-dimethylphenyl, 2, 4-dimethylphenyl, 2, 5-dimethylphenyl, 2, 6-dimethylphenyl, 3, 4-dimethylphenyl, 3, 5-dimethylphenyl, 2-methoxypheny, 3-methoxypheny, 4-methoxypheny, 4-ethoxy phenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxy phenyl, 4-hexyloxy phenyl, 2, 3-dimethoxy phenyl, 2, 4-dimethoxy phenyl, 2, 5-dimethoxy phenyl, 2, 6-dimethoxy phenyl, 3, 4-dimethoxy phenyl, 3, 5-dimethoxy phenyl, 3 and 4, 5-trimethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 4-BUROMO phenyl, 4-iodine phenyl, 4-fluoro phenyl, 4-(phenylthio) phenyl, 3-(phenylthio) phenyl, 2-(phenylthio) phenyl group, etc. can be illustrated.
[0036] Each following radical can be illustrated as a phenyl group which has had 1-3 of the radical chosen from a low-grade alkyl group, a lower alkoxy group, a halogen atom, a nitro group, a halogenation low-grade alkyl group, a halogenation lower alkoxy group, a low-grade alkoxy carbonyl group, hydroxyl, a phenyl lower alkoxy group, the amino group, a cyano group, a low-grade alkanoloxy radical, a phenyl group, and a JI low-grade alkoxy phosphoryl low-grade alkyl group as a substituent.
[0037] Namely, phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethyl phenyl, 4-propyl phenyl, 4-buthylphenyl, 4-t-buthylphenyl, 4-pentyl phenyl, 4-hexyl phenyl, 2-methoxypheny, 3-methoxypheny, 4-methoxypheny, 4-ethoxy phenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxy phenyl, 4-hexyloxy phenyl, 2, 3-dimethoxy phenyl, 2, 4-dimethoxy phenyl, 2, 5-dimethoxy phenyl, 2, 6-dimethoxy phenyl, 3, 4-dimethoxy phenyl, 3, 5-dimethoxy phenyl, 2 and 3, 4-trimethoxyphenyl, 2, 3, 5-trimethoxyphenyl, 2 and 3, 6-trimethoxyphenyl, 2, 4, 5-trimethoxyphenyl, 2 and 4, 6-trimethoxyphenyl, 3, 4, 5-trimethoxyphenyl, 3 and 4, 5-TORIETOKISHI phenyl, 2-fluoro phenyl, 3-fluoro phenyl, 4-fluoro phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-BUROMO phenyl, 3-BUROMO phenyl, 4-BUROMO phenyl, 4-iodine phenyl, 2, 3-dichlorophenyl, 2, 4-dichlorophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-trifluoro methylphenyl, 3-trifluoro methylphenyl, 4-trifluoro methylphenyl, 4-pentafluoroethyl phenyl, 4-heptafluoro propyl phenyl, 4-nona fluoro buthylphenyl, 4-undeca fluoro pentyl phenyl, 4-trideca fluoro hexyl phenyl, 2-methoxycarbonyl phenyl, 3-methoxycarbonyl phenyl, 4-methoxycarbonyl phenyl, 4-ethoxycarbonyl phenyl, 4-propoxy carbonylphenyl, 4-butoxycarbonyl phenyl, 4-pentyloxy carbonylphenyl, 4-hexyloxy carbonylphenyl, 2-biphenyl, 3-biphenyl, 4-biphenyl, 2-(diethoxy phosphoryl methyl) phenyl, 3-(diethoxy phosphoryl methyl) phenyl, 4-(diethoxy phosphoryl methyl) phenyl, 4-(dimethoxy phosphoryl methyl) phenyl, 4-

(diisopropoxy phosphoryl methyl) phenyl, 3, 5-dimethoxy-4-ethoxy phenyl, 3, 5-dimethoxy-4-propoxy phenyl, 4-butoxy - 3, 5-dimethoxy phenyl, 3, 5-dimethoxy-4-pentyloxy phenyl, 3, 5-dimethoxy-4-hexyloxy phenyl, 2, 3-bis(trifluoromethyl) phenyl, 2, 4-bis(trifluoromethyl) phenyl, 2, 5-bis (trifluoromethyl) phenyl, 2, 6-bis(trifluoromethyl) phenyl, 3, 4-bis(trifluoromethyl) phenyl, 3, 5-bis (trifluoromethyl) phenyl, 3, 5-dimethoxy-4-hydroxyphenyl, 3, 5-diethoxy-4-hydroxyphenyl, 3, 5-dipropoxy-4-hydroxyphenyl, 4-benzyloxy - 3, 5-dimethoxy phenyl, 4-benzyloxy - 3, 5-diethoxy phenyl, 3, 5-dimethoxy-4-(2-phenylethoxy) phenyl, 4-acetoxy -3, 5-dimethoxy phenyl, 3, 5-dimethoxy-4-propionyloxy phenyl, 2-chloro -3, 5-dimethoxy phenyl, 4-chloro -3, 5-dimethoxy phenyl, 4-BUROMO - 3, 5-dimethoxy phenyl, 3, 5-dimethoxy-4-iodine phenyl, 3, 5-dichloro-4-methoxypheny, 3, 5-dichloro-4-ethoxy phenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 4-trifluoro methoxypheny, 3-trifluoro methoxypheny, 2-trifluoro methoxypheny, 4-pentafluoro ethoxy phenyl, 4-heptafluoro propoxy phenyl, 4-nona fluoro butoxy phenyl, 4-undeca fluoro pentyloxy phenyl, 4-trideca fluoro hexyloxy phenyl, 3, 5-bis(trifluoro methoxy) phenyl, 3 and 4, 5-tris (trifluoro methoxy) phenyl group, etc. can be illustrated.

[0038] As a phenyl group which has had the phenylthio radical as a substituent, phenyl, 4-(phenylthio) phenyl, 3-(phenylthio) phenyl, 2-(phenylthio) phenyl group, etc. can be illustrated.

[0039] As benzoyl which has 1-3 of the radical chosen from a lower alkoxy group, a halogenation low-grade alkyl group, and a halogen atom as a substituent 2-chloro benzoyl, 3-chloro benzoyl, 4-chloro benzoyl, 2-fluoro benzoyl, 2-BUROMO benzoyl, 2-iodine benzoyl, 2, 4-dichlorobenzoyl, 3, 4-dichlorobenzoyl, 2, 5-dichlorobenzoyl, 2, 6-dichlorobenzoyl, 2-trifluoro methylbenzoyl, 3-trifluoro methylbenzoyl, 4-trifluoro methylbenzoyl, 3, 5-bis(trifluoromethyl) benzoyl, 3 and 4, 5-tris (trifluoromethyl) benzoyl, 2-methoxy benzoyl, 3-methoxy benzoyl, 4-methoxy benzoyl, 2, 3-dimethoxybenzoyl, 2, 4-dimethoxybenzoyl, 3, 5-dimethoxybenzoyl, 3, 4, 5-trimethoxybenzoyl, 2-ethoxy benzoyl, 2-propoxy benzoyl, 2-butoxy benzoyl, 2-pentyloxy benzoyl, 2-hexyloxy benzoyl, etc. can be illustrated.

[0040] As each radical in the general formula (2) showing the active principle of this invention adenosine enhancement agent, each following radical can be illustrated, for example. That is, as a low-grade alkyl group, straight chains, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, and a hexyl group, or a branched chain-like low-grade alkyl group can be illustrated.

[0041] As a low-grade alkylene group, methylene, ethylene, ethylidene, trimethylene, tetramethylen, pentamethylene, hexamethylene, etc. can be illustrated.

[0042] As a phenyl group which has 1-3 of a lower alkoxy group as a substituent 2-methoxypheny, 3-methoxypheny, 4-methoxypheny, 4-ethoxy phenyl, 4-propoxy phenyl, 4-butoxy phenyl, 4-pentyloxy phenyl, 4-hexyloxy phenyl, 2, 4-dimethoxy phenyl, 3, 4-dimethoxy phenyl, 3, 5-dimethoxy phenyl, 2 and 4, 5-trimethoxyphenyl, 3 and 4, 5-trimethoxyphenyl, 2 and 4, 6-trimethoxyphenyl, 4-ethoxy -3, 5-dimethoxy phenyl group, etc. can be illustrated.

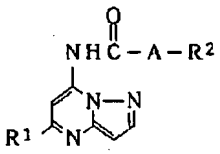
[0043] The [1 and 5-pyrazolo a] pyrimidine derivative expressed with a general formula (1) and (2) is useful to the therapy and prevention of myocardial infarction or cerebral infarction as an adenosine enhancement agent. And there is no side effect with this derivative common to the conventional adenosine enhancement agent, and it does not have a possibility of bringing about a hallucination, distraction, etc. or causing addiction and habituation, either.

[0044] As a [1 and 5-pyrazolo a] pyrimidine derivative desirable as the above-mentioned adenosine enhancement agent active principle, the compound of a general formula (2) and R4, and R5 and R6 can illustrate the compound of the general formula (1) single bond and whose n a carbonyl group and A are 0 for a hydrogen atom and Q.

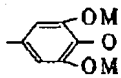
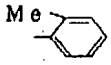
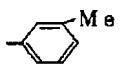
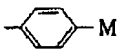
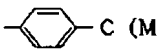
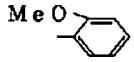
[0045] The compound of the general formula (1) which is the phenyl group in which (a) R2 have three of a lower alkoxy group as a substituent also especially among the desirable [1 and 5-pyrazolo a] pyrimidine derivatives, such as this, And the compound of the general formula (2) which is the phenyl group in which R22 has three of a lower alkoxy group as a substituent is more suitable. Also among them, it is R1. The compound of the general formula (1) which is n-propyl group or n-butyl, and especially the compound of the general formula (2) whose R11 is n-butyl are suitable.

[0046] As an example of the most desirable [1 and 5-pyrazolo a] pyrimidine derivative A 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine, A 5-n-propyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine, 5 pyrazolo [-n-butyl-2-methyl-7-(3, 4, 5-trimethoxy benzoylamino)] [1 and 5-a] pyrimidine, And a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoyloxy) pyrazolo [1 and 5-a] pyrimidine can be illustrated. The 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine is the optimal also among them.
[0047] this invention active principle compound expressed with a general formula (1) can be manufactured by various kinds of approaches, and can illustrate the approach of a publication as the example, for example in said WO 95/No. 35298 official report.
[0048] this invention active principle compound can be obtained by obtaining the 7-hydroxy [1 and 5-pyrazolo a] pyrimidines, carrying out the condensation reaction of suitable carboxylate and the 3-amino pyrazoles, halogenating this subsequently, carrying out to the 7-halogeno [1 and 5-pyrazolo a] pyrimidines typically, processing this by aqueous ammonia or the hydrazine further, changing into 7-amino object, and making a halogenide react to this.
[0049] this invention active principle compound expressed with a general formula (2) can also be manufactured by various kinds of approaches. As the example, the approach of a publication can be illustrated, for example in said WO 97/No. 11946 official report.
[0050] this invention active principle compound expressed with a general formula (2) can be obtained by obtaining the 7-halogeno [1 and 5-pyrazolo a] pyrimidines, and making the suitable, alcoholic derivative for this as well as the compound of the above-mentioned general formula (1) react typically.
[0051] In this way, as an example of the active principle compound of this invention adenosine enhancement agent obtained, each compound shown in the 1st table of the following - the 6th table as examples 1-136 can be illustrated.
[0052]
[Table 1]

第　1　表

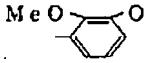
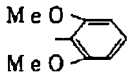
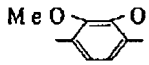
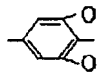
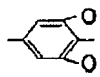
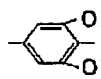
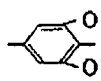


Me：メチル基、Et：エチル基、nPr：n－プロピル基、
nBu：n－ブチル基、nPe：n－ペンチル基、Ph：フェニル基

実施例No.	R^1	R^2	A	融　点（℃）（再結晶溶媒）
1	nBu		単結合	127～129（ジエチルエーテル－n－ヘキサン）
2	nBu	Ph	単結合	83～85（酢酸エチル－n－ヘキサン）
3	nBu		単結合	102～104（n－ヘキサン）
4	nBu		単結合	94～95（n－ヘキサン）
5	nBu		単結合	83～84（n－ヘキサン）
6	nBu		単結合	^{1}H－NMR（CDCℓ$_3$） 0.97(3H,t,J=7.3), 1.37(9H,s), 1.4-1.5(2H,m), 1.7-1.9(2H,m), 2.86(2H,t,J=7.8), 6.57(1H,d,J=2.3), 7.58(1H,d,J=8.7), 7.77(1H,s), 7.97(1H,d,J=8.7), 8.03(1H,d,J=2.3), 10.0(1H,brs)
7	nBu		単結合	82～84（n－ヘキサン）
8	nBu		単結合	49～51（n－ヘキサン）

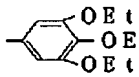
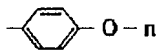
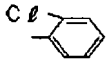
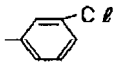
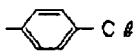
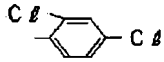
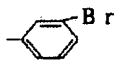
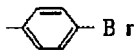
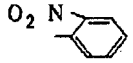
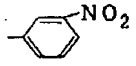
[0053]
[Table 2]

第 1 表 (続き)

実施例No.	R^1	R^2	A	融点 (℃) (再結晶溶媒)
9	nBu		単結合	108～109 (n－ヘキサン)
10	nBu		単結合	129～132 (n－ヘキサン)
11	nBu		単結合	143～144 (ジエチルエーテル－n－ヘキサン)
12	nBu		単結合	101～103 (ジエチルエーテル－n－ヘキサン)
13	nBu		単結合	92～94 (ジエチルエーテル－n－ヘキサン)
14	nBu		単結合	115～117 (酢酸エチル－n－ヘキサン)
15	Et		単結合	141～143 (酢酸エチル－n－ヘキサン)
16	nPr		単結合	119～121 (ジエチルエーテル－n－ヘキサン)
17			単結合	198～201 (酢酸エチル－n－ヘキサン)
18	nPe		単結合	116～118 (n－ヘキサン)
19	Ph		単結合	185～187 (酢酸エチル－n－ヘキサン)

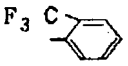
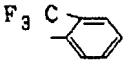
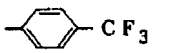
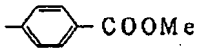
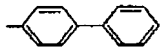
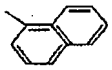
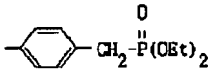
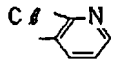
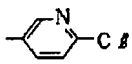
[0054]
[Table 3]

第 1 表 (続き)

実施例No.	R^1	R^2	A	融点 (℃) (再結晶溶媒)
20	nBu		単結合	100～102 (ジエチルエーテル－n－ヘキサン)
21	nBu		単結合	87～90 (n－ヘキサン)
22	nBu		単結合	99～100 (n－ヘキサン)
23	nBu		単結合	107～109 (ジエチルエーテル)
24	nBu		単結合	81～82 (n－ヘキサン)
25	nBu		単結合	92～94 (ジエチルエーテル)
26	nBu		単結合	97～99 (n－ヘキサン)
27	nBu		単結合	93～95 (n－ヘキサン)
28	nBu		単結合	97～99 (n－ヘキサン)
29	nBu		単結合	133～135 (酢酸エチル－n－ヘキサン)
30	nBu		単結合	143～145 (酢酸エチル－n－ヘキサン)

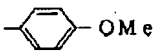
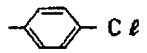
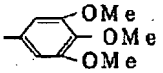
[0055]
[Table 4]

第 1 表 (続き)

実施例No.	R1	R2	A	融点 (℃) (再結晶溶媒)
31	Et		単結合	125～127 (ジエチルエーテル－n－ヘキサン)
32	nBu		単結合	84～87 (n－ヘキサン)
33	nBu		単結合	95～97 (n－ヘキサン)
34	nBu		単結合	122～123 (n－ヘキサン)
35	nBu		単結合	139～141 (酢酸エチル－n－ヘキサン)
36	nBu		単結合	119～121 (酢酸エチル－n－ヘキサン)
37	nBu		単結合	57～60 (酢酸エチル－n－ヘキサン)
38	nBu		単結合	82～84 (ジエチルエーテル－n－ヘキサン)
39	nBu		単結合	103～105 (酢酸エチル－n－ヘキサン)
40	nBu		単結合	92～93 (ジエチルエーテル－n－ヘキサン)
41	nBu	Ph	$-CH_2-$	80～82 (ジエチルエーテル－n－ヘキサン)

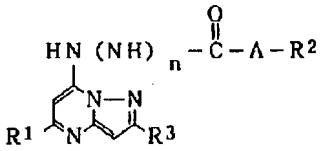
[0056]
[Table 5]

第 1 表 (続き)

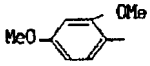
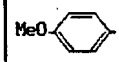
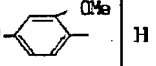
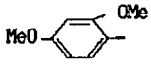
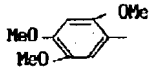
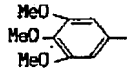
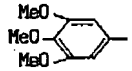
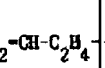
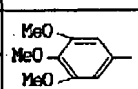
実施例No.	R^1	R^2	A	融点 (℃) (再結晶溶媒)
42	nBu		$-CH_2-$	73～75 (ジエチルエーテル－n－ヘキサン)
43	nBu	Ph	$-C_2H_4-$	^1H－NMR ($CDCl_3$) 0.95(3H,t,J=7.3), 1.3-1.5 (2H,m), 1.7-1.8(2H,m), 2.80 (2H,t,J=7.8), 2.88(2H,t,J=7.5), 3.09(2H,t,J=7.5), 6.53 (1H,d,J=2.2), 7.2-7.3(5H,m), 7.60(1H,s), 7.95(1H,d,J=2.2), 9.23(1H,brs)
44	nBu	PhO－	$-CH_2-$	108～109 (n－ヘキサン)
45	nBu		$-CH_2-$	140～142 (酢酸エチル－n－ヘキサン)
46	nBu		-CH=CH-	134～137 (酢酸エチル－n－ヘキサン)

[0057]
[Table 6]

第　2　表

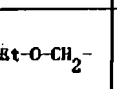
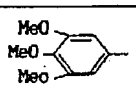
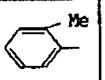
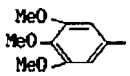
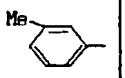
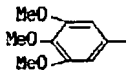
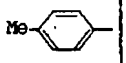
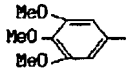
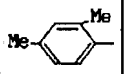
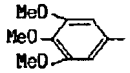
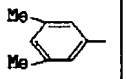
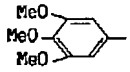
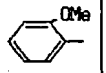
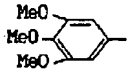
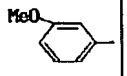
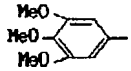
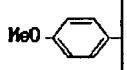
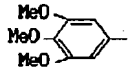
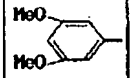
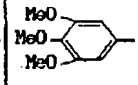
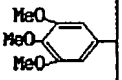
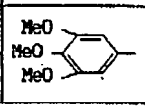


Me：メチル基、Et：エチル基、nPr：n－プロピル基、
nBu：n－ブチル基、tBu：t－ブチル基、nPe：n－ペンチル基、
Ph：フェニル基、Ac：アセチル基

実施例No.	R1	R2	R3	A	n	融点（℃）（再結晶溶媒）
47	nBu		H	単結合	0	^{1}H－NMR（CDCℓ$_3$） 0.95(3H,t,J=7.4), 1.2-2.1 (14H,m), 2.4-2.6(1H,m),2.81 (2H,t,J=7.8), 6.54(1H,d,J=2.2),7.62(1H,s), 8.00(1H,d, J=2.2),9.29(1H,brs)
48	nBu		H	単結合	0	141～142（エタノール－n－ヘキサン）
49			H	単結合	0	209～211（塩化メチレン－酢酸エチル）
50			H	単結合	0	206～208（塩化メチレン－酢酸エチル）
51	nBu		H	単結合	0	136～137（エタノール－n－ヘキサン）
52	Me		H	単結合	0	173～175（エタノール－n－ヘキサン）
53	nBu		Me	単結合	0	127～129（エタノール－n－ヘキサン）
54			H	単結合	0	104～106（酢酸エチル－n－ヘキサン）

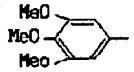
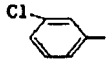
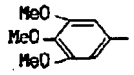
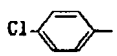
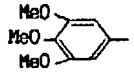
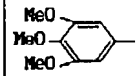
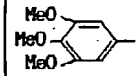
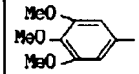
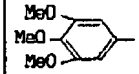
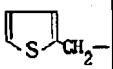
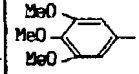
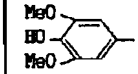
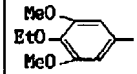
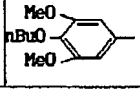
[0058]
[Table 7]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
55			H	単結合	0	138～140 (酢酸エチル－n－ヘキサン)
56			H	単結合	0	163～165 (クロロホルム－酢酸エチル)
57			H	単結合	0	166～168 (酢酸エチル－n－ヘキサン)
58			H	単結合	0	193～195 (塩化メチレン－ジエチルエーテル)
59			H	単結合	0	174～176 (塩化メチレン－ジエチルエーテル)
60			H	単結合	0	203～205 (塩化メチレン－ジエチルエーテル)
61			H	単結合	0	175～177 (塩化メチレン－酢酸エチル)
62			H	単結合	0	192～194 (塩化メチレン－ジエチルエーテル)
63			H	単結合	0	181～183 (塩化メチレン－ジエチルエーテル)
64			H	単結合	0	224～226 (塩化メチレン－ジエチルエーテル)
65			H	単結合	0	214～216 (塩化メチレン－ジエチルエーテル)

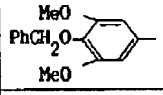
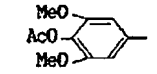
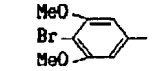
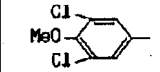
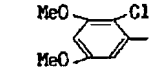
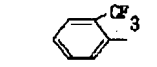
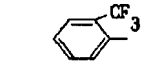
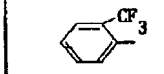
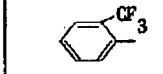
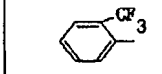
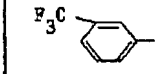
[0059]
[Table 8]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
66			H	単結合	0	190～192 (塩化メチレン－ジエチルエーテル)
67			H	単結合	0	222～224 (クロロホルム－酢酸エチル)
68			H	単結合	0	193～195 (クロロホルム－酢酸エチル)
69			H	単結合	0	189～191 (塩化メチレン－ジエチルエーテル)
70			H	単結合	0	174～176 (塩化メチレン－酢酸エチル)
71			H	単結合	0	191～193 (塩化メチレン－ジエチルエーテル)
72			H	単結合	0	198～200 (塩化メチレン－酢酸エチル)
73			H	単結合	0	157～159 (酢酸エチル)
74	nBu		H	単結合	0	159～161 (エタノール－n－ヘキサン)
75	nBu		H	単結合	0	79～81 (ジエチルエーテル－n－ヘキサン)
76	nBu		H	単結合	0	98～100 (n－ヘキサン)

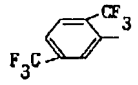
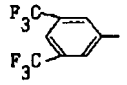
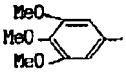
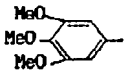
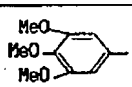
[0060]
[Table 9]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
77	nBu		H	単結合	0	82～85 (エタノール－n－ヘキサン)
78	nBu		H	単結合	0	158～160 (酢酸エチル－n－ヘキサン)
79	nBu		H	単結合	0	182～184 (酢酸エチル－n－ヘキサン)
80	nBu		H	単結合	0	132～135 (酢酸エチル－n－ヘキサン)
81	nBu		H	単結合	0	111～113 (ジエチルエーテル－n－ヘキサン)
82	Me		H	単結合	0	154～155 (エタノール－n－ヘキサン)
83	nPr		H	単結合	0	139～141 (ジエチルエーテル－n－ヘキサン)
84			H	単結合	0	102～104 (n－ヘキサン)
85	nPe		H	単結合	0	93～95 (n－ヘキサン)
86	Ph		H	単結合	0	143～145 (ジエチルエーテル－n－ヘキサン)
87	nBu		H	単結合	0	46～48 (酢酸エチル－n－ヘキサン)

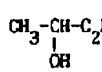
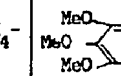
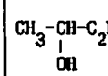
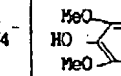
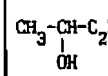
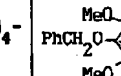
[0061]
[Table 10]

第 2 表 (続き)

実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
88	nBu		H	単結合	0	108～110 (n-ヘキサン)
89	nBu		H	単結合	0	92.5～94.5 (n-ヘキサン)
90	nBu		H	単結合	0	106～108 (n-ヘキサン)
91	nBu		H	単結合	0	123～125 (エタノール-n-ヘキサン)
92	nBu		H	単結合	0	123～125 (ジエチルエーテル-n-ヘキサン)
93	nBu		H	単結合	0	139～140 (エタノール-n-ヘキサン)
94	nBu		H	CH_2	0	121～123 (酢酸エチル-n-ヘキサン)
95	nBu		H	-CH=CH-	0	194～196 (エタノール-n-ヘキサン)
96	nBu		H	単結合	1	222 (分解) (エタノール-n-ヘキサン)
97	Ph		H	単結合	1	250 (分解) (メタノール-n-ヘキサン)
98	nBu		H	単結合	1	247 (分解) (エタノール-n-ヘキサン)

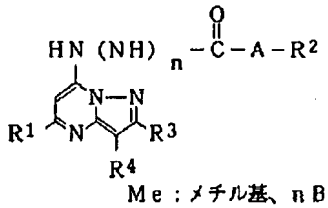
[0062]
[Table 11]

第 2 表 (続き)

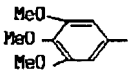
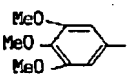
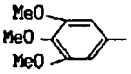
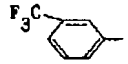
実施例No.	R1	R2	R3	A	n	融点 (℃) (再結晶溶媒)
99	Ph		H	単結合	1	263 (分解) (エタノール-n-ヘキサン)
100			H	単結合	0	128～130 (塩化メチレン-n-ヘキサン)
101			H	単結合	0	153～155 (エタノール-n-ヘキサン)
102			H	単結合	0	127～129 (酢酸エチル-n-ヘキサン)

[0063]
[Table 12]

第 3 表

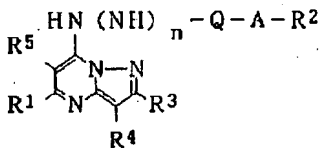


Me：メチル基、nBu：n－ブチル基、

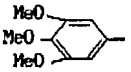
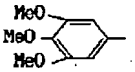
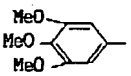
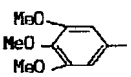
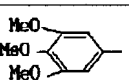
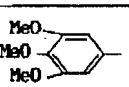
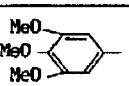
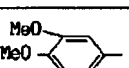
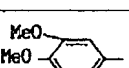
実施例No.	R^1	R^2	R^3	R^4	A	n	融点（℃）（再結晶溶媒）
103	nBu		Me	Cl	単結合	0	106～108（エタノール－n－ヘキサン）
104	nBu		H	Cl	単結合	0	142～143（エタノール－n－ヘキサン）
105	nBu		H	Br	単結合	0	146～148（エタノール－n－ヘキサン）
106	nBu		H	Cl	単結合	0	133～135（ジエチルエーテル－n－ヘキサン）

[0064]
[Table 13]

第　4　表

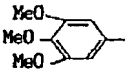
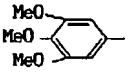
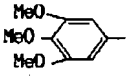
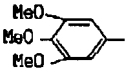
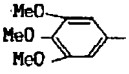
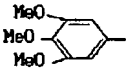
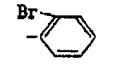
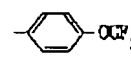
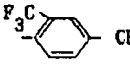
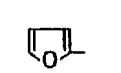
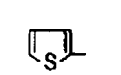


Me：メチル基、Et：エチル基、nBu：n－ブチル基、Ph：フェニル基

実施例No.	R^1	R^5	R^2	R^3	R^4	Q	A	n	融点（℃）（再結晶溶媒）
107	H	H		H	H	O ‖ C	単結合	0	185～187（塩化メチレン－n－ヘキサン）
108	nBu	H		Me	O ‖ -COEt	O ‖ C	単結合	0	138～140（酢酸エチル－n－ヘキサン）
109	nBu	H		nBu	H	O ‖ C	単結合	0	95～97（酢酸エチル－n－ヘキサン）
110	nBu	H		nBu	Me	O ‖ C	単結合	0	96～98（酢酸エチル－n－ヘキサン）
111	nBu	H		Ph	H	O ‖ C	単結合	0	190～192（塩化メチレン－ジエチルエーテル）
112	nBu	H		Ph	$PhCH_2$-	O ‖ C	単結合	0	149～151（酢酸エチル n－ヘキサン）
113	nBu	H		Ph	PhS 	O ‖ C	単結合	0	111～113（酢酸エチル－n－ヘキサン）
114	nBu	H		H	nBu	O ‖ C	単結合	0	81～83（n－ヘキサン）
115	nBu	H		H	Ph	O ‖ C	単結合	0	139～141（酢酸エチル－n－ヘキサン）

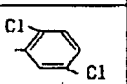
[0065]
[Table 14]

第 4 表 (続き)

実施例No.	R1	R5	R2	R3	R4	Q	A	n	融点 (℃) (再結晶溶媒)
116	nBu	Me		H	H	O ‖ C	単結合	0	145～147 (塩化メチレン－n－ヘキサン)
117	$-CH_2CH_2CH_2CH_2-$			H	H	O ‖ C	単結合	0	102～104 (塩化メチレン－n－ヘキサン)
118	$Me-\overset{\overset{O}{\|}}{C}-CH_2CH_2-$	H		H	H	O ‖ C	単結合	0	115～117 (塩化メチレン－n－ヘキサン)
119	$Et-S-CH_2-$	H		H	H	O ‖ C	単結合	0	80～82 (酢酸エチル－n－ヘキサン)
120	$MeS-CH_2CH_2-$	H		H	H	O ‖ C	単結合	0	113～115 (塩化メチレン－ジエチルエーテル)
121	PhS-	H		H	H	O ‖ C	単結合	0	179～181 (塩化メチレン－ジエチルエーテル)
122	nBu	H		H	H	O ‖ C	単結合	0	98～100 (ジエチルエーテル)
123	nBu	H		H	H	O ‖ C	単結合	0	73～75 (n－ヘキサン)
124	nBu	H		H	H	O ‖ C	単結合	0	129～131 (n－ヘキサン)
125	nBu	H		H	H	O ‖ C	単結合	0	91～93 (ジエチルエーテル n－ヘキサン)
126	nBu	H		H	H	O ‖ C	単結合	0	91～93 (n－ヘキサン)

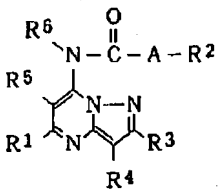
[0066]
[Table 15]

第 4 表 (続き)

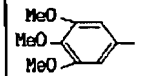
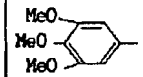
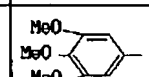
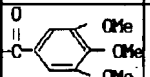
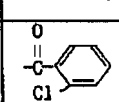
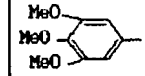
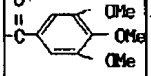
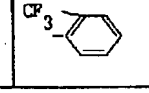
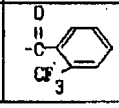
実施例No.	R1	R5	R2	R3	R4	Q	A	n	融点 (℃) (再結晶溶媒)
127	nBu	H	Ph	H	H	SO_2	単結合	0	300℃以上 (酢酸エチル－n－ヘキサン)
128	nBu	H		H	H	SO_2	単結合	0	300℃以上 (酢酸エチル－n－ヘキサン)

[0067]
[Table 16]

第 5 表

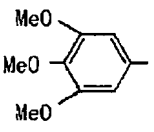


Me：メチル基、nBu：n－ブチル基

実施例No.	R1	R5	R2	R3	R4	R6	A	融点 (℃) (再結晶溶媒)
129	nBu	H		H	H	Me	単結合	93～95 (酢酸エチル－n－ヘキサン)
130	nBu	H		H	H	Ph-CH_2-	単結合	^{1}H-NMR($CDCl_3$) 0.76(3H,t,J=7.2), 0.9-1.1(2H,m), 1.3-1.4(2H,m), 2.51(2H,t,J=7.4), 3.47(6H,s), 3.74(3H,s), 5.33(2H,brs), 5.83(1H,s), 6.60(2H,s), 6.68(1H,d,J=2.0), 7.1-7.3(5H,m), 8.24(1H,d,J=2.0)
131	nBu	H		H	H		単結合	127～129 (酢酸エチル－n－ヘキサン)
132	nBu	H		H	H		単結合	119～121 (ジエチルエーテル－n－ヘキサン)
133	Me	H		H	H		単結合	180～182 (塩化メチレン－n－ヘキサン)
134	nBu	H		H	H		単結合	111～113 (ジエチルエーテル－n－ヘキサン)

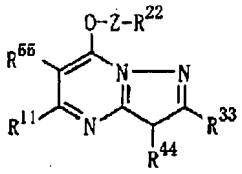
[0068]
[Table 17]

第 5 表 (続き)

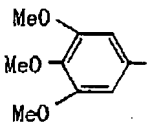
実施例No.	R1	R5	R2	R3	R4	R6	A	融点 (℃) (再結晶溶媒)
135	HOOC-C_3H_6-	H		H	H	H	単結合	191-193 (エタノール-n－ヘキサン)

[0069]
[Table 18]

第 6 表



Me：メチル基、n－Bu：n－ブチル基

実施例No.	R^{11}	R^{22}	R^{33}	R^{44}	R^{55}	Z	融 点 (℃) (再結晶溶媒)
136	n-Bu		H	H	H	$-CH_2-$	100-103 (酢酸エチル-n－ヘキサン)

[0070] Each compound expressed with a general formula (1) and a general formula (2) can be made into the acid addition salt permitted in physic, and salts, such as this, are also included by the active principle compound of this invention adenosine enhancement agent. As an acid in which the above-mentioned acid addition salt may be made to form, organic acids, such as inorganic acids, such as a hydrochloric acid, a hydrobromic acid, and a sulfuric acid, oxalic acid, a fumaric acid, a maleic acid, a tartaric acid, and a citric acid, can be illustrated, for example, and the formation reaction of this acid addition salt can follow a conventional method.

[0071] Moreover, the inside of the compound expressed with a general formula (1) and R6 What is a hydrogen atom can make this copper salt, such as alkaline-earth-metal salts, for example, a calcium salt, such as an alkali-metal salt, for example, sodium salt, and potassium salt, and magnesium salt, etc. according to a conventional method, and salts, such as this, are also included by the active principle compound of this invention adenosine enhancement agent.

[0072] In addition, the inside of the compound expressed with a general formula (1), the compound whose A is an alkenylene group, and R1 Some compounds which are low-grade alkenyl radicals can take cis- ** trans-isomer structure, and this invention adenosine enhancement agent can make all, such as this, an active principle.

[0073] Moreover, the optical isomer which made the carbon atom the asymmetric center exists in the part in the compound expressed with a general formula (1), and this invention adenosine enhancement agent can make an active principle both this optically active substance and racemic modification.

[0074] This is used for this invention adenosine enhancement agent with suitable avirulent pharmaceutical preparation support by making into an active principle at least one sort chosen from the compound expressed with the compound and general formula (2) which are expressed with a general formula (1), and it is made into the gestalt of a common physic pharmaceutical preparation constituent, and is used.

[0075] A diluent or excipients, such as the bulking agent usually used according to the use gestalt of pharmaceutical preparation as the above-mentioned pharmaceutical preparation support used for this invention physic pharmaceutical preparation, an extending agent, a binder, moisture adhesive material, disintegrator, a surface active agent, and lubricant, can be illustrated, and selection use of these is suitably carried out according to the administration unit form voice of the pharmaceutical preparation obtained.

[0076] As administration unit form voice of the above-mentioned physic pharmaceutical preparation, various kinds of gestalten can choose according to the therapy purpose, and a tablet, a pill, powder, liquids and solutions, suspension, an emulsion, a granule, a capsule, suppositories, injections (liquids and solutions, suspension, etc.), an ointment, etc. are mentioned as the typical thing.

[0077] It faces fabricating in the gestalt of a tablet. As the above-mentioned pharmaceutical preparation

support For example, a lactose, White soft sugar, a sodium chloride, grape sugar, a urea, starch, a calcium carbonate, Excipients, such as a kaolin, crystalline cellulose, a silicic acid, and potassium phosphate, water, Ethanol, propanol, simple syrup, grape-sugar liquid, starch liquid, A gelatin solution, a carboxymethyl cellulose, hydroxypropylcellulose, Binders, such as methyl cellulose and a polyvinyl pyrrolidone, carboxymethylcellulose sodium, Carboxymethyl-cellulose calcium, hydroxypropylcellulose, Desiccation starch, sodium alginate, agar powder, the end of a laminaran, Disintegrator, such as a sodium hydrogencarbonate and a calcium carbonate, and polyoxyethylene sorbitan fatty acid ester Surfactants, such as sodium lauryl sulfate and a stearic acid monoglyceride, Collapse inhibitors, such as white soft sugar, stearin, cocoa butter, and hydrogenated oil, a quarternary-ammonium-salt radical, Lubricant, such as a polyethylene glycol, etc. can be used in adsorbents, such as moisturizers, such as absorption enhancers, such as sodium lauryl sulfate, a glycerol, and starch, starch, a lactose, a kaolin, a bentonite, and a colloid silicic acid, purification talc, a stearate, and the end of a boric acid. Furthermore, a tablet can be used as the tablet which gave the usual coating if needed, for example, a sugar-coated tablet, a gelatin encapsulation lock, an enteric tablet, a film coated tablet or an auxiliary rim lock, and a multilayered tablet.

[0078] It faces fabricating in the gestalt of a pill and disintegrator, such as binders, such as excipients, such as grape sugar, a lactose, starch, cacao butter, hardening vegetable oil, a kaolin, and talc, gummi arabicum pulveratum, powdered tragacanth, gelatin, and ethanol, a laminaran, and agar, etc. can be used as pharmaceutical preparation support.

[0079] It faces fabricating in the gestalt of suppositories and the ester of a polyethylene glycol, cacao butter, higher alcohol, and higher alcohol, gelatin, semisynthetic glyceride, etc. can be used as pharmaceutical preparation support.

[0080] A capsule is mixed with various kinds of pharmaceutical preparation support which usually illustrated the active principle compound of this invention above according to the conventional method, and is filled up with and adjusted to a hard gelatine capsule, an elasticity capsule, etc.

[0081] When prepared as injections, such as liquids and solutions, an emulsion, and suspension, it can be sterilized, and as for this etc., it is desirable that they are blood and an isotonicity, and it is faced fabricating in gestalten, such as this, and can use water, ethyl alcohol, macro gall, propylene glycol, ethoxylation isostearyl alcohol, polyoxy-ized isostearyl alcohol, and polyoxyethylene sorbitan fatty acid ester as a diluent. In addition, the salt, the grape sugar, or the glycerol of sufficient amount to adjust an isosmotic solution in this case may be made to contain in this invention drugs, and the usual solubilizing agent, a buffer, an aponia-ized agent, etc. may be added.

[0082] Furthermore, a coloring agent, a preservative, perfume, a flavor agent, a sweetening agent, etc. and other drugs can also be made to contain in this invention drugs if needed.

[0083] It faces fabricating in the gestalt of ointments, such as a paste, a cream, and gel, and white vaseline, a paraffin, a glycerol, a cellulosic, a polyethylene glycol, silicon, a bentonite, etc. can be used as a diluent.

[0084] Although especially the amount of the active principle compound expressed with the general formula (1) and general formula (2) which should be contained in this invention drugs is not limited but is suitably chosen from a large area, it is usually good in physic pharmaceutical preparation to contain about about 1 to 70% of the weight.

[0085] Especially the medication method of the above-mentioned physic pharmaceutical preparation does not have a limit, and is determined according to various formulation, a patient's age, the conditions of sex and others, extent of a disease, etc. for example, a tablet, a pill, liquids and solutions, suspension, an emulsion, a granule, and a capsule administer orally -- having -- injections -- independent -- or it mixes with the usual water additions, such as grape sugar and amino acid, and administers intravenously -- having -- further -- the need -- responding -- independent -- the inside of intramuscular and a hide, and hypodermically -- or intraperitoneal administration is carried out and intrarectal administration of the suppositories is carried out.

[0086] Although the dose of the above-mentioned physic pharmaceutical preparation is suitably chosen by the direction for use, a patient's age, the conditions of sex and others, extent of a disease, etc., it is

good for the amount of this invention compound which is usually an active principle to set to about about 0.5-20mg per weight per day of 1kg, and it can prescribe this pharmaceutical preparation for the patient in 1 - 4 steps on the 1st.

[Translation done.]

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

EXAMPLE

[Example] Hereafter, in order to explain this invention in more detail, the example of preparation of this invention adenosine enhancement agent is given, and, subsequently the example of a pharmacological test is given.
[0088]
[The example 1 of preparation] The hard gelatine capsule (1000 pieces) contained 250mg per capsule was prepared by the next formula, using a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine as a preparation active principle compound of a capsule.
[0089]
An active principle compound 250g crystalline cellulose (Japanese pharmacopoeia article) 30g corn starch (Japanese pharmacopoeia article) 17g talc (Japanese pharmacopoeia article) 2g magnesium stearate (Japanese pharmacopoeia article) 1g, i.e., each component, was finely used as powder, the gelatine capsule for internal use which has a desired dimension after mixing was enough filled up so that it might become a homogeneous mixture, and the target capsule was prepared.
[0090]
[The example 2 of preparation] The tablet (2000 locks) contained 300mg per one lock was prepared by the next formula, using a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine as a preparation active principle compound of a tablet.
[0091]
An active principle compound 600g lactose (Japanese pharmacopoeia article) 67g corn starch (Japanese pharmacopoeia article) 33g carboxymethyl-cellulose calcium (Japanese pharmacopoeia article) 25g methyl cellulose (Japanese pharmacopoeia article) 12g magnesium stearate (Japanese pharmacopoeia article) According to 3g, i.e., the above-mentioned formula, an active principle compound, a lactose, corn starch, and carboxymethyl-cellulose calcium are mixed enough. Mixture was granulated using the methyl cellulose water solution, the screen of 24 meshes was mixed with through, this was mixed with magnesium stearate, it pressed in the tablet, and the target tablet was prepared.
[0092]
[The example 1 of a pharmacological test] The Hartley (Hartley) system male guinea pig (10 weeks old, 400-450g) was slaughtered by cervical dislocation, the ileum was taken out, and the surrounding organization was exfoliated. The ileum was carved into die length of 3-4cm, it hung under the pressure of 1g during the organ bath which put in 10ml (NaCl 118mM, KCl 4.7mM, CaCl2 2.5mM, KH2PO4 1.2mM, MgSO4 1.2mM, NaHCO3 25mM, glucose 11mM) of Krebs-Henseleit solutions, and aeration of the O2-/CO2 (95% / 5%) mixed gas was carried out continuously.
[0093] Adding the electrical stimulation of 25V to this ileum with the period of 0.1Hz, the adenosine was cumulatively added from 10-8M during the organ bath, and it asked for the adenosine concentration by which the twitch Mr. contraction by electrical stimulation is controlled 100% (control group).
[0094] In addition, twitch Mr. contraction was measured in AISO tonic transformer DEYUSA (isotonic transducer, the Nihon Kohden make, TD-111T), and was recorded by the recorder (NIHON DENSI KAGAKU, U-228).

[0095] On the other hand, 30 quotas which add an adenosine were asked for the adenosine concentration which adds during the organ bath and by which the twitch Mr. contraction by electrical stimulation is controlled [M / 10-6M (this invention group 1) or / (this invention group 2) / 3x10-6] 100% in a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine like the above.
[0096] Consequently, the adenosine concentration by which contraction is controlled 100% was set to 10-6M by this invention group 1, and was set to 3x10-7M by this invention group 2, and it fell to 1/3 and 1/10 compared with the control group, respectively. this invention active principle compound became clear [that the outstanding adenosine potentiation is shown] from this.
[0097]
[The example 2 of a pharmacological test] The Hartley (Hartley) system male guinea pig (10 weeks old, 400-450g) was slaughtered by cervical dislocation, the heart was taken out, and the atrium was separated. this after checking that the atrium has contracted spontaneously -- a Krebs-Henseleit solution (NaCl [ ] -- 118 mM) KCl 4.7 -- mM and CaCl2 2.5mM and KH2PO4 1.2 mM MgSO4 1.2 -- mM and NaHCO3 25mM and glucose It hung under the pressure of 1g during the organ bath which put in 10ml of 11mM(s), and aeration of the O2-/CO2 (95% / 5%) mixed gas was carried out continuously.
[0098] The adenosine was cumulatively added from 3x10-7M during the organ bath, and it asked for the adenosine concentration by which spontaneous contraction of an atrium begins to be controlled (control group).
[0099] In addition, spontaneous contraction of an atrium was measured in AISO tonic transformer DEYUSA (isotonic transducer, the Nihon Kohden make, TD-111T), and after amplifying with living body amplifier (Nihon Kohden, TB-611T), it was recorded by the recorder (NIHON DENSI KAGAKU, U-228).
[0100] On the other hand, ten quotas which add an adenosine were asked for the adenosine concentration which adds during the organ bath and by which spontaneous contraction of an atrium begins to be controlled [M / 3x10-6M (this invention group 1) or / (this invention group 2) / 10-5] in a 5-n-butyl-7-(3, 4, 5-trimethoxy benzoylamino) pyrazolo [1 and 5-a] pyrimidine like the above.
[0101] Consequently, the adenosine concentration by which contraction begins to be controlled 100% was set to 3x10-7M by this invention group 1, and was set to 10-7M by this invention group 2, and it fell to 1/10 and 1/30 compared with the control group, respectively. this invention active principle compound became clear [that the outstanding adenosine potentiation is shown] from this.
[0102]
[The example 3 of a pharmacological test] The longitudinal muscle was exfoliated, after having slaughtered the Hartley (Hartley) system male guinea pig (10 weeks old, 350-400g) by cervical dislocation, taking out the ileum and removing contents and an unnecessary organization. The longitudinal muscle which exfoliated was attached in the cannula which fixed the electrode, aeration of the O2-/CO2 (95% / 5%) mixed gas was carried out, and it hung in Magnus tubing which filled the Krebs-Henseleit solution (NaCl 118.3mM, KCl 4.7mM, CaCl2 2.5mM, KH2PO4 1.2mM, MgSO4 1.2mM, NaHCO3 25.0mM, glucose 11.1mM) which kept it warm at 37 degrees C. In addition, the longitudinal muscle prevented from touching a direct electrode.
[0103] When SUTIMYURETA (diamond medical system company make, DPS-06 mold) was used for the above-mentioned longitudinal muscle, the electrical stimulation of the square wave for period [of 0.1Hz] and persistence time 0.5 m seconds was added and nerve-stimulus contraction was stabilized, the adenosine was cumulatively added from 0.1microM in the Krebs-Henseleit solution, and IC50 of nerve-stimulus contraction depressant action was calculated.
[0104] The IC50 above-mentioned value was calculated from the adenosine concentration of two points, and the rate of control before and after 50% of rates of control. In addition, nerve-stimulus contraction was measured using FD pickup (the Nihon Kohden Corp. make, TB-611T mold) and amplifier (the Nihon Kohden Corp. make, AP-601G mold).
[0105] On the other hand, as a sample offering compound, it adds to five quotas which add an adenosine by the concentration of 1microM by using as a dimethyl sulfoxide solution the compound shown in said each table, and they were asked for IC50 of the nerve-stimulus contraction depressant action of an

adenosine like the above. And whenever [enhancement] was computed by having calculated the ratio of IC50 at the time of sample offering compound un-adding to this value.
[0106] A result is shown in the 7th table of the following.
[0107]
[Table 19]

供試化合物(実施例番号)	増強度
1	4．8
16	7．6
19	6．9
53	8．4
55	5．1
75	6．0
100	2．7
111	2．7
135	2．6
136	7．1

[0108] this invention active principle compound became clear [that the outstanding adenosine potentiation is shown] from the above-mentioned table.

[Translation done.]